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## A COMPARISON OF THE METABOLIC EFFECTS OF ISOCALORIC MEALS OF VARYING COMPOSITION, WITH SPECIAL REFERENCE TO THE PREVENTION OF POSTPRANDIAL HYPOGLYCEMIC SYMPTOMS\*

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### INTRODUCTION

EFFICIENCY experts have long recognized the desirability of supplying intermediate supplementary nourishment to maintain the performance of office and factory personnel throughout the working day. Insufficient attention has been given to the fact that the ingestion of a typical American breakfast—one relatively high in carbohydrate and low in protein and fat content—predisposes to midmorning hypoglycemic symptoms. Similarly a luncheon of relatively high carbohydrate content predisposes to hypoglycemia in the midafternoon. During these periods of relative hypoglycemia a definite impairment in performance may be expected. Provision of supplementary nourishment is obviously indicated during these periods except in the case of obese individuals. Circumstances, however, sometimes render the provision of intermediate nourishment either impractical or impossible. Furthermore in certain occupations involving excessive or continued physical labor the ingestion of food without a rest period may initiate undesirable sequelae in some individuals.

The prolonged sense of well-being which follows the ingestion of a meal rich in protein suggested that the intake of increased protein at breakfast might obviate the necessity for midmorning nourishment and might be expected to improve the performance of individuals who do not have ready access to supplementary nourishment at that time. Conn and Newburgh<sup>1</sup>

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From the Department of Medicine, Harvard Medical School, and the Peter Bent Brigham Hospital, Boston.

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have reported that blood sugar levels fluctuate widely following the ingestion of a high carbohydrate meal, whereas little or no change in blood sugar level was observed following the ingestion of a high protein meal. These authors employed diets which provided equivalent quantities of theoretically available glucose. The caloric value of the high protein meal used in their studies was approximately double that of the high carbohydrate meal.

With these considerations in mind, studies were undertaken to determine the changes in blood sugar level, caloric distribution, and metabolic rate which followed the ingestion of *isocaloric* breakfasts composed of varying proportions of carbohydrate, fat and protein.

#### METHODS

This study was carried out on a normal male subject who had been trained for respiratory studies. For a period of 48 hours prior to each experimental period he was fed a diet composed of carbohydrate 304 gm., protein 69 gm., and fat 113 gm. (2509 calories). Following a 14-hour fast, blood sugar level, standard metabolic rate, respiratory quotient and urinary nitrogen excretion were measured. The subject was then given one of the test meals which was consumed within 10 minutes. He remained in bed throughout the experimental period. At hourly intervals after the ingestion of the meal for a period of six hours, blood was taken and urine obtained for analysis. The last 10 minutes of each hour were spent in collecting the subject's expired air in a modified Baily gasometer. Air samples were analyzed in duplicate for oxygen and carbon dioxide by means of a Haldane-Henderson gas analyzer. Differential derivation of calories was made with the aid of Lusk's table.<sup>2</sup> Blood sugar was determined according to the method of Folin and Malmros<sup>3</sup> and urinary nitrogen by a modified micro-Kjeldahl method.

The diets employed in this study were isocaloric but of varying carbohydrate, protein and fat composition (table 1). The actual foods used in these diets are presented in tables 2, 3 and 4.

TABLE I  
Isocaloric Breakfasts

	CHO gm.	Protein gm.	Fat gm.	Total Calories
High CHO.....	82	9	4	400
High Protein.....	26	55	8	396
High Fat.....	20	8	32	400

#### OBSERVATIONS

Administration of a high carbohydrate breakfast resulted in a definite increase in the blood sugar level in one hour, followed by a rapid fall to a level of 69 mg. per 100 c.c. at the end of two hours. The fall in blood sugar



TABLE II  
High Carbohydrate Breakfast

Item	Quantity gm.	CHO gm.	Protein gm.	Fat gm.	Calories
Orange juice.....	200	20	2	0	88
Cornflakes.....	12	10	2	0	48
Sugar.....	9	9	0	0	36
Bread.....	50	26	4	0	120
Butter.....	4	0	0	3	27
Jelly.....	20	15	0	0	60
Milk.....	30	2	1	1	21
Total.....	—	82	9	4	400

TABLE III  
High Protein Breakfast

Item	Quantity gm.	CHO gm.	Protein gm.	Fat gm.	Calories
Skim milk.....	400	20	14	3	163
Lean beef.....	30	0	7	3	55
Cottage cheese.....	160	6	34	2	178
Total.....	—	26	55	8	396

TABLE IV  
High Fat Breakfast

Item	Quantity gm.	CHO gm.	Protein gm.	Fat gm.	Calories
Cornflakes.....	18	15	3	0	72
Cream 19 per cent.....	160	5	5	32	328
Total.....	—	20	8	32	400

level was associated with hunger and weakness. Following this episode, the blood sugar level gradually returned to normal (chart 1). Administration of a high protein meal of the same caloric value, on the other hand, was followed by a definite sense of well-being and a maintenance of normal blood sugar level throughout the six-hour experimental period (chart 1). Following a high fat meal, blood sugar levels fell more slowly than after the high carbohydrate meal, reaching a low level of 71 mg. in five hours. Hypoglycemic symptoms were noted following the high fat breakfast, but were less severe than following the high carbohydrate meal, and occurred much later (chart 1). There was a striking rise in metabolic rate one hour after the high carbohydrate meal followed by a return to basal level in two hours. After the ingestion of the high protein meal the metabolic rate remained elevated throughout the experimental period. The ingestion of the high fat meal had little influence on metabolic rate (chart 2).

### CHANGES IN BLOOD SUGAR FOLLOWING VARIOUS ISOCALORIC MEALS

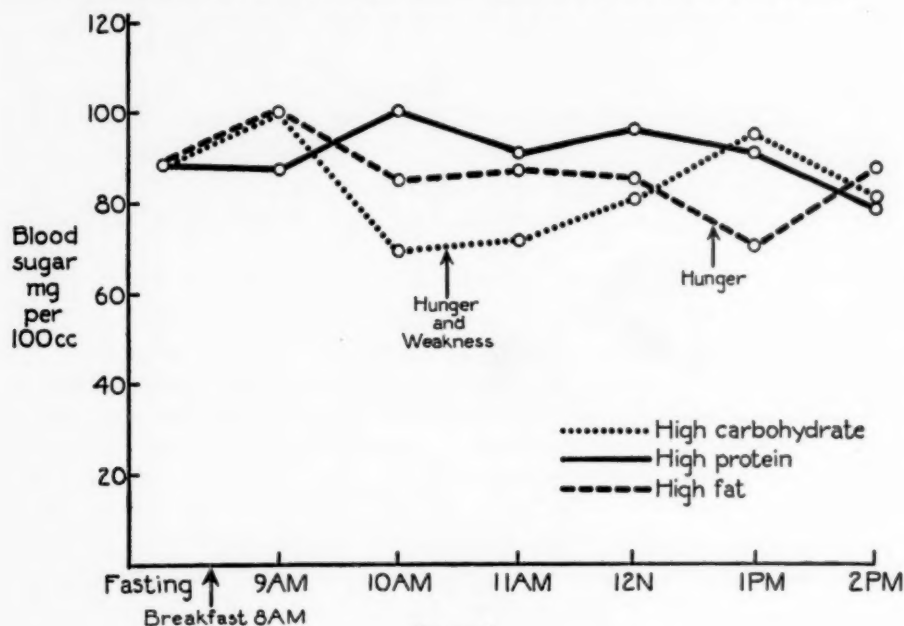


CHART 1.

### CHANGES IN METABOLIC RATE FOLLOWING VARIOUS ISOCALORIC MEALS

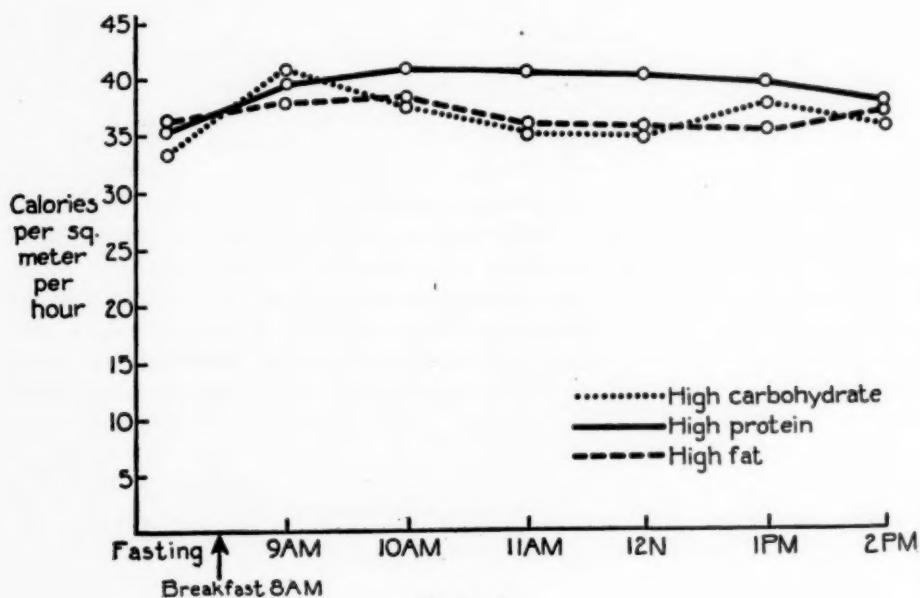


CHART 2.

Differential derivation of calories following the ingestion of the various meals is depicted in chart 3. One hour after the ingestion of the high carbohydrate breakfast there was a decided increase in the percentage of total calories derived from carbohydrate; during the remainder of the period, however, there was a gradual decrease in the percentage of calories derived from carbohydrate. The percentage of calories derived from fat increased greatly during the last half of the experimental period. The percentage of

### CALORIC CHANGES FOLLOWING VARIOUS ISOCALORIC MEALS

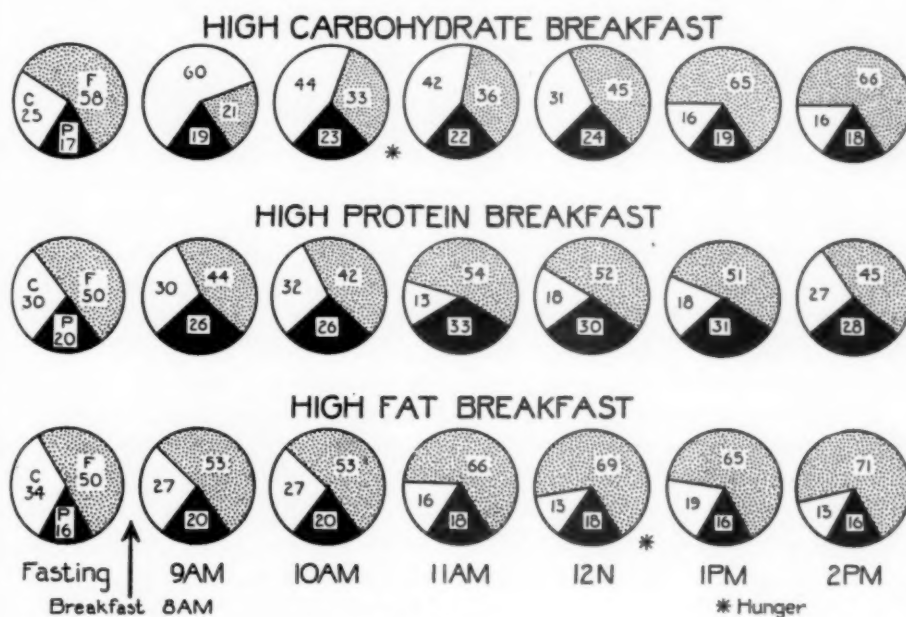


CHART 3.

calories derived from protein changed but little following the high carbohydrate meal.

Following the ingestion of the high protein meal, a decided increase was noted in the percentage of calories derived from protein. This increase persisted throughout the entire six-hour period. Calories derived from carbohydrate decreased throughout this study, whereas calories derived from fat changed relatively little.

A gradual increase in the percentage of calories derived from fat followed the ingestion of the high fat breakfast. This was associated with a gradual decrease in the calories derived from carbohydrate. No significant change occurred in the percentage of calories derived from protein.

## DISCUSSION

Hypoglycemic symptoms are experienced by many individuals two to three hours following meals; symptoms are most likely to occur following the ingestion of a meal of high carbohydrate content. Differential derivation of calories following the high carbohydrate meal used in these studies disclosed a rapid change from predominantly carbohydrate metabolism to predominantly fat metabolism during the second to third hour. This change was taking place at the time hypoglycemic symptoms occurred. It is probable that the inability of many individuals to effect a rapid and smooth transition from a metabolic state involving the utilization of carbohydrate to one utilizing fat as the major source of energy results in the occurrence of hypoglycemic symptoms during this transition.

The occurrence of postprandial hypoglycemic symptoms is known to result in loss of efficiency, and it would appear to be desirable to provide intermediate nourishment at this time for workers despite loss of time and difficulties involved in making suitable arrangements. In some occupations, however, it is not possible to provide intermediate nourishment even though the desirability of such a procedure is evident. The ingestion of a meal of predominantly carbohydrate content, followed in two to three hours by hypoglycemic symptoms which are in turn relieved by the ingestion of more carbohydrate, may result in the establishment of a vicious circle which in turn may lead to obesity. The benefits which might be derived from increased protein in the diet under these circumstances are apparent.

The advantages of employing a diet high in fat and high in protein in the treatment of patients with spontaneous hypoglycemia have been pointed out by Waters,<sup>4</sup> Clark and Greene,<sup>5</sup> Conn,<sup>6</sup> and Swanson and Greene.<sup>7</sup> The sustained increase in metabolic level which follows the ingestion of protein, in contrast to carbohydrate, may also be advantageous. That a diet of high protein content is not harmful to a normal individual has been demonstrated in a convincing manner by Stefanson<sup>8</sup> who lived in this country for one year on a diet consisting almost entirely of protein and fat.

The limitation of protein as a source of food for the duration of the war makes the provision of a high protein diet a practical impossibility, but does not prevent the substitution of moderate quantities of protein for carbohydrate in every day diet. For the obese individuals skim milk and cottage cheese may be used advantageously; whole milk, cheese, nuts and soy bean meal may be used in the diets of nonobese individuals.

## CONCLUSIONS

1. In a normal subject the ingestion of a breakfast high in carbohydrate and low in protein and fat was followed by hypoglycemic symptoms in one to two hours; an isocaloric breakfast high in fat and low in carbohydrate and protein was followed by hypoglycemic symptoms at a later hour; an

isocaloric breakfast high in protein and low in fat and carbohydrate was followed by an improved sense of well-being and no symptoms of hypoglycemia. The blood sugar levels following these three breakfasts corresponded closely to the clinical symptoms.

2. A sustained increase in metabolic rate occurred following the ingestion of the high protein breakfast; a transient increase in metabolic rate followed by a fall below the basal metabolic rate was observed after the ingestion of an isocaloric high carbohydrate breakfast; no significant increase in metabolic level followed the ingestion of an isocaloric high fat breakfast.

3. Following the ingestion of the high carbohydrate breakfast, differential derivation of calories reflected striking fluctuations in the character of the food substances utilized as sources of energy. These fluctuations did not occur following the isocaloric high protein and high fat meals.

4. The disadvantages which may attend the ingestion of meals preponderantly carbohydrate in content are discussed and the possible advantages of an increased protein content are suggested.

The authors are indebted to Miss Marion J. Brian, dietitian in charge of the Metabolic Unit of the Peter Bent Brigham Hospital, for her assistance in this study.

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## THE PROBLEMS OF THE INTERNIST IN THE NAVY \*

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Most of the problems which are to be discussed will seem commonplace and in civil practice they would probably be routine matters. However, when considered in the light of the requirements of strenuous and arduous military duties, they present additional issues for the consideration and decision of the internist.

In general, the problems of the naval internist fall into three main categories. First, those concerned with the proper physical selection of personnel, or the elimination of applicants for the service showing physical defects which are of present or may be of future significance. Secondly, the maintenance of physical fitness among our entire personnel. This includes the management and treatment of illness developing in our men, in accordance with the very best medical practice. And thirdly, problems entailing a decision as to whether or not certain diseases are of sufficient import to warrant the retirement of individuals in whom they develop.

The maintenance of an efficient Navy demands personnel who are in the very best of physical condition. It is the duty of our recruiting officers to exercise the greatest of care in selecting personnel. Many medical conditions which are of no great consequence under the ordinary demands of civil pursuits may be of considerable moment when the individual is subjected to the rigorous and exacting duties of naval life. Pulmonary tuberculosis in a preclinical, quiescent or arrested stage is a notable example of such a condition. In civil life, these lesions may never cause disability, but under military conditions involving strenuous physical exertion, long hours and sustained effort and residence in tropical climates, they almost invariably break down.

The importance of incipient hypertension in the naval forces cannot be exaggerated. The medical examiner is repeatedly confronted with the question of accepting a candidate who is otherwise perfectly normal, often of unusually fine physique, whose blood pressure tends to be somewhat elevated. It is appreciated that excitement elevates arterial tension and that is why examiners are directed to take a number of readings under varying conditions. On the other hand, a patient possessing a definite hypertension may at times present a normal blood pressure reading. In fact, the blood pressure of hypertensives is notoriously labile. We know, however, that if the blood pressure rises to abnormal heights it may mean actual hypertension, prehypertension or potential hypertension.

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Can we afford to turn down the borderline or mild hypertensive in time of war when millions are needed for our military forces? We all know that this man will be good for even most strenuous physical activity for years before definite hypertension appears or becomes a fact. However, if the Navy accepts this candidate and if his blood pressure increases because of the natural course of the disease, the finding of a definite hypertension after the man has been in the service for some time can, by present laws, be construed as caused by or aggravated by service in the Navy. In the case of an officer he will be retired with three quarters of his base pay for the rest of his life. These few remarks show the peculiar angles of the question of incipient hypertension in the Navy.

The question as to the significance of the systolic murmur heard over the mitral or apical regions is ever with the medical examiner. In civilian practice, if after a thorough work up the internist cannot decide whether the murmur is of functional or organic origin, he advises the patient to return for reexamination the next day, week or month, and meanwhile permits the man to carry on all routine physical activities. Not so in the Navy, the examiners may have to decide immediately in case the candidate has come from afar, and usually without the benefit of the electrocardiograph, stethocardiograph, fluoroscope or kymograph. He has to take the full responsibility of deciding the origin of this suspicious systolic murmur in spite of the fact that at times it is quite difficult to make a decision, and when in fact there is still no completely sure way of deciding its origin.

Many other problems having to do with the exclusion of the unfit have to be solved. Is the albuminuria noted in the otherwise desirable young applicant benign or does it have a pathological significance? The question as to the importance of a persistent tachycardia or a cardiac arrhythmia must be carefully evaluated. The consideration of these and other conditions found in applicants for the Naval Service are very practical matters with which the internist must be concerned.

The naval internist plays only a modest part in maintenance of physical fitness among our personnel. The officer trained in public health and sanitation has a much wider field, finding and perfecting methods for the control of epidemic and infectious diseases. In the Navy every officer and man must be physically fit to perform his duties at all times, in all places and under any conditions. Nothing disrupts organization on board ship more than men on the sick list. Take for example a gun crew on any of our ships; here we find team work in its highest state of efficiency. Every man is a specialist in his assigned task. The gun pointer spends many hours finding means to increase the speed with which he can get on his target. The gun captain works to find ways of correlating his group so that extra salvos may be put in the air. The training of this crew takes months. Should some of these men become frequent visitors to the sick list the efficiency of the whole group is gone.

In the management and treatment of the sick our problems are, with few exceptions, no different from those in civil life. Our hospitals are all equipped with every modern facility for proper diagnostic study, therapeutic management and nursing attention. I believe that our naval hospitals furnish the finest example of group practice. There is no cut-throat competition and a helpful coöperative spirit prevails. Our hospital ships and base units are likewise very well equipped, and it is only on small ships on independent duty and some few small outlying stations that the internist may have to rely on his five senses and ingenuity alone. The four quarters of the globe are covered by our Navy and the internist must have a working knowledge of the diseases common to both the tropics and the arctics. He must keep abreast of modern methods of prevention and treatment of these tropical diseases which are of naval importance. The tropical diseases of greatest importance at present which are apt to become of increasing importance are:

- Malaria (including Blackwater Fever)
- Dengue
- Dengue-like fevers (Sand Fly Fever)
- Dysenteries, both bacillary and amebic

Those of potential importance which may become disabling to naval personnel are:

- Typhus and other rickettsial diseases
- Cholera
- Yellow fever
- Plague
- The relapsing fevers
- Infectious jaundice and other leptospiroses
- Oroya fever

In our combatant areas, both the African and Southwest Pacific, malaria is more important than all the rest of these tropical diseases combined. The Bureau of Medicine and Surgery has just distributed to all medical officers a pamphlet "Notes on Tropical and Exotic Diseases of Naval Importance." It is well to become acquainted with the treatment of malaria as outlined in this brochure, as the shortage of quinine is rapidly becoming critical.

Although every effort is made to place the highly specialized internist in our larger hospitals where his special training and knowledge will be of most value, this is not always possible. He must realize that although he may have been a heart specialist in civil life, he is now entering another specialty, military medicine, and must adapt himself to it.

I now come to the last group, i.e., those considered for retirement. This is the one in which the problem of the internist in the service and the internist in civil life diverge. One of the most difficult problems the Naval internist has to contend with and one that calls for ability, judgment and service ex-

perience is the question of invaliding from the service many desirable members whose training and experience are invaluable to the service.

One of the most distressing things that has come to our attention in the past 20 years is the apparent increase in coronary heart disease. The management of the typical coronary case has a different aspect in the naval service. In civilian life the patient frequently finds it no hardship when told to let up a bit and lead a sensible life. He doesn't lose out and usually adjusts himself very quickly. On the other hand, we have made a hard and fast rule among our officers that no one who has had a frank coronary attack can return to active duty. This may seem cruel and some of you may feel that we are wasting valuable officer material. Consider then the responsibility that falls upon an officer, especially of the line of the Navy. Speed is the essence of everything today. Our ships go faster, our planes fly at increasing speeds. This means that the officer in command of units, or a single unit must have his faculties alert at all times. I can leave it to your imagination what would happen to a number of ships in column, traveling at a speed of 30 knots, should the Commanding Officer of this division or the Commanding Officer of a single unit collapse at his station on the bridge at the time the command was passed to change the course of the formation. It is for this reason that we cannot allow an officer who has had one serious heart attack to assume these spots of great responsibility.

Other types of cardiovascular disease present very much the same picture. How much stress and strain should we allow the individual who has cardiac valvular disease or who is carrying a very high diastolic pressure? How long should we permit this man to go before we call a halt and return him to civil life where he can be rehabilitated in a normal fashion?

Another type of case that is of particular concern to the internist is the peptic ulcer, usually duodenal. The majority of these cases just do not do well in the naval service. There is always the difficulty of obtaining the proper diet and the threat of hemorrhage or perforation. They usually seek duty where they can secure both diet and medical advice. Even after surgery they invariably come back to the internist. These cases eventually have to be invalided from the Service.

The naval internist is against continuing on the active list those individuals requiring substitution therapy, for example hypothyroid states, diabetes, pernicious anemia, or those requiring maintenance doses of drugs such as digitalis and quinidine. In other words, a man who has to depend on a bottle of medicine for his efficiency is not a top flight officer.

In our larger hospitals we are gradually divorcing syphilis and skin from the medical services. This brings up the subject of "Line of Duty" which is most important to every officer and man when he enters upon the sick list. His retired pay or pension will depend upon his ability to establish his line of duty status. The doctor must fairly judge his cases and see that no in-

justices are done and that no means are overlooked to aid patients in clearing up delicate points which may mean everything to them in the future.

During our rapid expansion some men have been accepted who have disabilities that later are brought to light. The question as to whether these existed prior to enrollment or whether they were aggravated by service conditions has to be decided. In fairness both to the Government and the man, much thought must be given to these matters.

At this point, this question may properly be asked. What are we going to do with the officers or men with years of service who have great ability and experience? Are their services to be completely thrown away and lost to the Navy? The answer is "Yes" so far as the active list is concerned. However, in times of emergency such as the present one, we have adopted a system which is not unlike that used in civil life. A certain number of these officers and men are recommended for "spot jobs." By spot jobs we mean carefully selected duties in which a man can give the Navy the benefit of his ability and years of experience without subjecting him to the stress and strain of high responsibility. Every attempt is made to keep their duties within the limits of their physical capacity. At a time like this, the Nation and the Navy have the first call on service personnel, whether active or retired, but we as doctors try not to lose sight of the fact that the officer or man also has some equity and that we must consider the dependents of these men.

In time of peace the internist is given every opportunity as he goes along to increase his professional efficiency by postgraduate work in our civil institutions. In this connection, the Navy is especially grateful to the men, mostly Fellows of the College, who have helped train our internists in the field of cardiology, endocrinology, gastroenterology and respiratory diseases. In time of war, these courses are of necessity limited as to number and are shortened. However, it is the policy of the Bureau of Medicine and Surgery to be sure our internists attend as many of the clinics throughout this country as it is physically possible for them to do.

The Medical Department of the Navy is now in a much better position to carry on with its many vital research problems. On October 12, 1942, our new Research Institute was placed in commission as a unit of the National Naval Medical Center in Bethesda, Maryland. It is a magnificent building and contains every type of equipment necessary for scientific research. We were most fortunate in being able to obtain the services of Dr. A. C. Ivy, Professor of Physiology and Pharmacology at Northwestern, as Director of Research for our Institute. In addition to its well trained staff we have the coöperation and active participation of the leading scientists of the country through the medium of the Medical Division of the National Research Council. For reasons of security, I am not at liberty to discuss the many problems under investigation, but I can assure you that they are all most important and pertinent to the war effort, and will result in the saving of many lives.



In this brief review, I have merely attempted to give you an idea of what the internist in the Navy must do in addition to treating his patients. In the past two years our Corps has been augmented by many outstanding internists from all sections of the country. Many are now chiefs of the medical services in our hospitals. All have rapidly adjusted to Service conditions and are doing a splendid job.

Reports coming in from all areas indicate that the Medical Department of the Navy is functioning in a smooth and efficient manner. Just before leaving Washington I saw a report showing that of all the casualties evacuated from the Solomon Islands by plane to other bases, the mortality was less than 1 per cent. Reports coming from our hospital ships and mobile hospital bases located in remote sections of the world have been most gratifying. Yes—we in the Navy face the coming months and years with optimism and confidence in our ability to meet the tasks ahead. We do this with the sure knowledge that we will continue to receive the wholehearted coöperation and support of the American College of Physicians and the profession as a whole.

## MEDICAL CARE OF AVIATION PERSONNEL \*

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THE opportunity to speak before the regional meeting of the American College of Physicians, an organization so well known for its pioneer work in elevating and improving the standards of medical practice, is indeed a pleasure. Your college has offered recognition to physicians attaining a certain degree of proficiency, and at the same time, which is perhaps more important, has provided through its scientific sessions and its publications, invaluable postgraduate instruction.

Due to the efforts of such organizations, American medicine has indeed made phenomenal advances. Since 1900, the total death rate per 100,000 has been reduced nearly 50 per cent. Deaths from diphtheria have decreased from a rate of 43.5 to 2; typhoid fever from 36 to 1.9; pneumonia from 203 to 80; tuberculosis from 202 to 40. Each year brings notable advances in the prevention and treatment of diseases. Most of you can remember the treatment of diabetes without insulin; pernicious anemia without liver extracts; hemolytic streptococcal infections without sulfanilamide; pneumonia without oxygen, antiserum or the sulfonamides; and the deficiency diseases without specific vitamins. The chapter detailing the control and prevention of yellow fever and malaria is known to all of you. These represent but a few of the advances made in our own lifetime. The list of unsolved medical problems is still long, but they are being solved at an accelerated pace.

With the great need for qualified physicians to meet the present emergency, the Army Air Forces and other components of the armed services have been obliged to draw heavily upon your membership. At present, there are 125 of your fellows and associates in service with the Army Air Forces. You will, undoubtedly, wish to know what your associates are doing and how their services are being utilized. The special training of each physician entering the Air Forces, as indicated by internships, residencies, teaching and hospital affiliations, membership in the various specialty societies, colleges and boards, is carefully evaluated. Following a period of indoctrination and basic training, he is assigned to duty where his training can best be utilized. The Air Forces hospitals, of which there are several hundred (over 400), vary in size from a few beds to those of 2000 beds and more. The chief of the medical, surgical, orthopedic, laboratory, and other professional services, together with many of the younger men on each service, are selected individually. A well-balanced staff is set up, thus utilizing every physician in that field for which he is best qualified. Furthermore, as the organization of these hospitals is perfected, applications will be made to place them on the

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approved list for residencies. Many of our young physicians who have had postgraduate training interrupted, will thus be allowed to continue in recognized postgraduate work, at least for a time. Every effort is being made to encourage young medical officers to take the various boards and colleges while in service. A directive is being sent to the commanding officer of each Air Forces hospital, encouraging the granting of short leaves of absence for the purpose of taking these examinations. Whereas the older men and highly trained specialists will work largely in the hospitals, many of the younger ones will have the opportunity of studying at the School of Aviation Medicine, Randolph Field, Texas. Subsequent to graduation from this school, a year of further experience and training, under supervision, is required before the rating of flight surgeon may be obtained.

War brings to each physician in America the obligation to serve his country in whatever rôle he can best serve, but war also offers a challenge to the physicians of this country to solve its many complex problems. The last war, undoubtedly, emphasized many new medical emergencies, some of which were eagerly studied, investigated, and solved. The pandemic of influenza which swept the world during 1917 and 1918 was a tremendous stimulus to scientific endeavor and research on respiratory diseases. Encephalitis appeared and demanded clinical and laboratory investigation, which furthered the knowledge of this dreaded malady. Even the importance of measles as a serious disease, and the problem of its epidemiology was impressed upon all. The first knowledge regarding the virulence and fatalities occurring in streptococcal pneumonia was acquired during the last war. The many deaths that resulted from gas gangrene stimulated the laboratory workers to prepare its antitoxin. The general interest and recognition of obscure cardiovascular problems were accelerated, and an almost new terminology evolved. Vasomotor instability, effort syndrome, soldier's heart, and neurocirculatory asthenia became common phrases in the medical wards. Exceptional opportunities arose for the study of neuropsychiatric diseases, particularly in the field of functional disorders.

Out of the war came also the stimulus for airplane development, which dramatically demanded that the horizon of medicine be widened to include the almost limitless stratosphere. When man adapts himself to the air and is subjected to great speed, rapid changes in altitude and temperature, and sustained periods at high altitude, numerous physiological disturbances occur. Psychological hazards are present also. Each member of the flying crew faces the possibility of sudden death from the day his training begins. Facing death in the heat of battle is far different, psychologically, from enduring the fear of it during the many months of training. Thus, necessity gave birth and sanction to aviation medicine.

A tremendous amount of work is now being done in the Air Forces Classification Centers in an attempt to evaluate prospective members of the flying crew. The purpose is to select those men with special physical and mental

qualifications, resistant to these stresses. Oxygen indoctrination programs and low-pressure chamber research work is progressing and has already added a tremendous fund of knowledge, invaluable in the care of the flying crew. When the best qualified candidates for the flying crew have been selected and training instituted, the never-ending struggle to adjust man to his new environment begins. Part of this adjustment is accomplished by improved mechanical flying equipment, and part by conditioning the crew both physically and emotionally. The flight surgeon must be keenly aware of the many medical problems peculiar to the flying crew. He must be able to differentiate and interpret the various components of flying fatigue. Flying fatigue is difficult to define, but its results are obvious. It may produce indifference or excitement, fear or bravado, loss of confidence, slowing of reaction time, all of which contribute to accidents and failures in accomplishing a specific mission. It may, generally, be defined as the sum total of physical and emotional disturbances felt by each member of the flying crew. This must be interpreted individually, as it varies widely. It consists of the actual physical fatigue, the stress of psychological hazards, the monotony and boredom of the training grind, unpleasant living conditions, lack of recreation, irregular hours, insufficient sleep due to operational necessity or excessive personal indulgence, physiological changes due to altitude or flying conditions, and probably many more factors. These stresses affect not only the psychologically unstable individual, but are manifest in all members of the crew in varying degrees. The flight surgeon must detect and identify these symptoms early, correcting the particular phase of fatigue involved. In short, he must live, eat, play, and fly with the crew to fulfill properly his rôle as physician, father-confessor, and friend, for it is upon him that the responsibility rests of keeping the crew fit to fly.

Air evacuation of casualties is another phase of aviation medicine which will play a considerable rôle in this war. Studies are being made with regard to the types of cases which can be moved by air and to what altitudes. It must be determined how soon casualties of various types can be evacuated to this country, thus saving personnel, supplies, and shipping. That large numbers of troops, both ground and air forces, will be moved in this manner is certain. This is but another of a thousand pioneer problems undertaken by the Army Air Forces.

Today, this challenge to physicians is greater than during the last war for the opportunity now is unique. Never before in history has a thoroughly mixed population, taken from all sections of this country, been transported to every distant corner of the world. The diseases, epidemics, and medical problems of all countries, climates, and peoples are now ours to solve. Let every physician in America, whether he serves his country with the armed forces or at home, accept this challenge, and though his sacrifice is great, make his contribution to the advancement of medical knowledge during this crisis.

## PEPTIC ULCER IN THE UNITED STATES NAVY\*

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THIRTY-FIVE years ago the Surgeon General of the Navy listed in his Annual Report but two admissions to the sick list under gastric ulcer, or "ulcus gastricum" as it was then termed in the official nomenclature. Since that time there has been a steady rise in the incidence of all peptic ulcers. Thus, five duodenal and 21 gastric ulcers were listed in 1912, and 28 duodenal and 35 gastric ulcers in 1920.

In the accompanying table (table 1) the trend of U. S. Navy admission rates for duodenal ulcer is shown from 1924 up to the last prewar year,

TABLE I  
Admission Rates per 100,000. Ulcer, duodenum. U. S. Navy

1924.....	41	1933.....	123
1925.....	62	1934.....	136
1926.....	79	1935.....	145
1927.....	89	1937.....	114
1928.....	95	1938.....	91
1929.....	104	1939.....	92
1932.....	110	1940.....	117

1940. Kantor<sup>1</sup> gives somewhat different figures for the U. S. Army, asserting that in 1930 the admission rate for duodenal ulcer was 110, rising to 160 in 1939. Just why the Army should have a higher rate than the Navy for the same peacetime decade is not clear. Nor is it clear why in 1935 the Navy had its highest rate of ulcer admissions.

The most recent statistics available are those contained in the Annual Report of the Surgeon General of the U. S. Navy for the year 1940. As will be seen in table 2, ulcer, duodenum, ranks seventh among diseases of the digestive system in admissions to the sick list, but it ranks first in number of sick days per case.

Of the 305 peptic ulcers reported, 15 per cent were gastric ulcers. This high incidence of gastric ulcer is identical with that given by Allison and Thomas<sup>2</sup> for the Royal Navy in the same year, but it is markedly at variance with the recently reported findings of Chamberlin<sup>3</sup> and Berk<sup>4</sup> of the U. S. Army, and Urquhart and his associates<sup>4</sup> of the Canadian Expeditionary Force. For gastric ulcers constituted less than 5 per cent of the peptic ulcers in each of the latter series.

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(NOTE: Authorization has been obtained from the Surgeon General for publication.)

The writers of this paper wish to state that the opinions and assertions contained herein are private ones and are not to be construed as official or reflecting the views of the Navy Department or the naval service at large.



TABLE II  
Class 3. Diseases of the Digestive System. U. S. Navy, 1940

Disease	Number of New Admissions	Admission Rate per 100,000	Sick Days per Case
1. Gastroenteritis, acute.....	2282	1126	5.1
2. Appendicitis, acute.....	2263	1117	22.8
3. Hemorrhoids.....	678	335	17.2
4. Appendicitis, chronic.....	630	311	25.9
5. Gastritis, acute.....	554	273	7.7
6. Cholangitis, acute.....	480	237	22.0
7. Ulcer, duodenum.....	238	117	57.1
Ulcer, stomach.....	39	19	49.7
Ulcer, duodenum, perforated.....	22	11	56.4
Ulcer, stomach, perforated.....	6	3	—
All peptic ulcers.....	305	155	—

Had all the peptic ulcer patients of the Navy in 1940 been concentrated in one hospital, a ward of 47 beds would have been occupied continuously throughout the year. Further, peptic ulcer in 1940 occasioned the invaliding from the service of 20 per cent of those admitted with this disease, 61 enlisted men and 7 officers—more invalidings from the service than from asthma, or diabetes, or rheumatic fever, or arterial hypertension, or nephritis. Similarly, the British medical writers have stressed the seriousness of the peptic ulcer problem in the armed forces. Sir Arthur Hurst stated that “dyspepsia” in 1940 accounted for 17 per cent of all admissions to the military hospitals of England, and in May 1941 an editorial in the *Canadian Medical Association Journal* went so far as to state that peptic ulcer was the major disability of wartime.

Palmer<sup>7</sup> has recently reviewed the British figures and compared them to the findings of our own Army surgeons. There is a remarkable similarity in the statistical facts, and, in essence, they find that digestive diseases account for about 15 per cent of all medical patients admitted to military hospitals; of

TABLE III  
Ulcer Cases in Military Hospitals. (British figures from Brockbank<sup>2</sup>; United States and Canadian figures from Chamberlin,<sup>8</sup> Berk,<sup>9</sup> and Urquhart<sup>4</sup>)

Author	Hospital	Total G.I. Admissions	% Ulcer	% Duodenal
<b>British</b>				
Allison and Thomas.....	Naval	100	45	85
Brockbank.....	Military	931	42.5	84
Graham and Kerr.....	Military	246	64	85
Maingot.....	General	256	56	89
Morris.....	Military	500	50	—
Payne and Newman.....	E.M.S.	287	89	80
Spillane.....	Military	200	32	84
Willcox.....	E.M.S.	41	69	73
<b>United States and Canadian</b>				
Chamberlin.....	Lawson Gen.	316	31	95
Berk.....	Tilton Gen.	113	43	94
Urquhart.....	15th Can. Gen.	—	—	96

these, about 40 to 50 per cent are due to peptic ulcer; and of these ulcers, the British find that 85 per cent are duodenal, whereas the Americans and Canadians report 96 per cent duodenal. The exact figures are given in table 3.

#### PEPTIC ULCER IN THE PHILADELPHIA NAVAL HOSPITAL

The admission rate for peptic ulcer cases among active service men\* in this hospital is not higher than 1 per cent, but even though our series is small, it may be profitable to review the experience of the staff with the ulcer patients who have come to us in the eight war-months ending September 30, 1942. Our data are summarized in tables 4 and 5.

TABLE IV  
Peptic Ulcer at the Philadelphia Naval Hospital,  
8 months ending September 30, 1942

Ulcer, duodenum.....	23 cases (85%)
a. Perforated.....	4
b. Hemorrhage.....	1
Ulcer, stomach.....	4 cases (15%)
Total Peptic Ulcers.....	27 cases (100%)
Ulcers existing prior to entry.....	8 (30%)
Officers with ulcer.....	3
Enlisted men with ulcer.....	24

TABLE V  
Disposition of Peptic Ulcer Patients, U. S. N. H., Philadelphia,  
8 months ending September 30, 1942

Discharged to duty.....	7	(Officers 0, CPO 1, Men 6)
Limited to duty ashore only.....	5	(Officers 2, CPO 3, Men 0)
Invalided from the service.....	15	(Officers 1, CPO 1, Men 13)
Total.....	27	(Officers 3, CPO 5, Men 19)

On reviewing the service records of the group, several types stand out:

1. The recruit whose very entry into the service precipitates his ulcer. With no prior ulcer history, his symptoms appear within one month.
2. The recruit who has failed to recognize his previous ulcer episodes. His symptoms appear within six months.
3. The recruit who knows he has an ulcer, and who invariably remarks: "No one asked me if I had an ulcer when I enlisted." (One man had a six inch upper right rectus scar, the result of a perforation in 1932.)
4. Men who have served the Navy for some time and develop an ulcer in the normal course of events.
5. The retired chief petty officer who is called back to active duty at an age when readjustment is not easy.

The three officers with whom we had to deal fell into the first and fourth categories.

\* In contrast to U. S. Veteran Administration patients who have a high admission rate for peptic ulcer.

Table 5 records the disposition of our 27 cases. Three of the invalidings represented errors of judgment in previous discharges to duty. One officer and one of the men, sent back to duty after satisfactory response to treatment, relapsed within one week. One retired chief petty officer, who had been called back to active duty, developed an ulcer late in 1941, but he improved after hospitalization and was sent to limited shore duty. In three weeks he relapsed and had to be retired unfit for mobilization afloat or ashore.

#### THE DISPOSITION OF ULCER PATIENTS IN MILITARY MEDICINE

Disposition of the ulcer patient in the naval service is entrusted to the medical officer in charge of the case, provided he feels that the man is fit to return to duty. Otherwise he must submit the facts to a Board of Medical Survey which makes recommendations, subject to the approval of the Bureau of Medicine and Surgery.

As we have seen, in past years only 20 per cent of those suffering from ulcer have been invalided from the U. S. Naval Service. The British, early in the war, according to Brockbank,<sup>3</sup> sent most of the men who responded to treatment back to duty. However, so many relapsed that the War Office had to issue a ruling in the letter of February 1, 1941, giving these causes for invaliding from service: (1) A long chronic history of ulcer indigestion, with anemia, loss of weight, or tenderness (roentgen-ray confirmation not obligatory). (2) Active symptoms, with a lesion proved by roentgen-ray. (3) A history of perforation or massive hemorrhage.

Urquhart<sup>4</sup> of the Canadian Expeditionary Force, after having had the unpleasant experience of readmitting, within three months, 26 out of 40 men sent back to duty, came to the conclusion that "all cases of active duodenal ulcer should be invalided." Smellie,<sup>5</sup> in a recent article, agrees with him, saying: "Whenever the diagnosis of ulcer has been established, the soldier should be invalided, and returned to civilian life in the shortest possible time."

Chamberlin<sup>6</sup> of the Lawson General Hospital in Atlanta states: "The man with a peptic ulcer is unfit for military service." On his hospital service, all the enlisted men with ulcer and 16 out of 18 officers with ulcer were invalided from the Army. Only two officers were retained for assignment to limited duty.

Palmer,<sup>7</sup> on the other hand, feels that "under proper conditions, patients with peptic ulcer are capable of performing many important tasks. Hence they may be assigned to limited duty within the continental United States, under conditions permitting them to carry on such dietary and other therapy as may be necessary."

Allison and Thomas<sup>2</sup> of the Royal Navy distinguish between different types of ulcer cases. They state that "when pain is characteristic, and has recurred over a long period, there are strong reasons for invaliding," and "that men who have suffered from hemorrhage or perforation, even if recovery is complete, should be invalided." Otherwise they feel that patients

who have done well under treatment may be returned to duty with recommendation for shore service or for ships carrying a medical officer.

#### DISCUSSION

What then should be our policy in dealing with the ulcer problem in the United States Navy? First, we must make greater efforts to discover and eliminate the man who has a peptic ulcer before his entry into the service. This can be accomplished only through the diligence of the medical officers who are charged with the examination of prospective naval personnel. Recent health records have carried this sworn statement: "I hereby certify that I do not suffer from venereal disease, bed-wetting, asthma, hay fever, rheumatism, fits or insanity, flat or low arches." Would it not be well to add ulcer and chronic indigestion?

It would be folly for us to ignore the experience of the British and make the mistakes against which we have been warned. This will mean that whereas formerly we sent 80 per cent of our ulcer patients back to duty in peacetime, we must now exercise the utmost caution in discharging these men even to limited duty. It is our belief that the best interests of both the patient and the naval service demand that no officer or enlisted man, suffering from peptic ulcer, should be discharged to duty without the recommendation of a Board of Medical Survey, approved by the Bureau of Medicine and Surgery. The Board of Medical Survey, further, should recommend for return to duty only those ulcer patients who are definitely indispensable and whose case histories are most innocuous.

In considering the question of fitness for duty, it must be remembered that response to treatment in the hospital is not sufficient justification for making a prognosis. Will power to resist some of the pleasures of leave and liberty, intelligence sufficient to follow a convalescent ulcer diet at the regular mess, and emotional stability are elementary requisites for the exceptional case of healed peptic ulcer whom we may, with any degree of hope, send back to full duty. For this reason, before discharge we feel that it is wise to allow the man liberty several times, and, after the principles of the ulcer diet have been explained to him, to insist that he choose his food in the regular mess for some time. Patients who have had a perforation, a massive hemorrhage, or gastric surgery should, probably, always be invalidated from the service.

Occasionally the urgency of the times may justify risking a recurrence. As an illustration, we were about to recommend the discharge of a man from the service, when, by chance, one of his officers called to see him. We were informed that this patient was one of 20 men capable of teaching the repair of a secret precision instrument. Had we deprived the Navy of his services, many hundreds of lives might have been lost. Likewise, Officers and Chief Petty Officers who have special skills acquired from long naval service are not to be discarded lightly in these times. They should be considered for

limited duty ashore, where they may live with their families and run no greater risk of recurrence than if they were in civilian life.

Aside from these special cases, there is little reason for retaining the ulcer patient, whether he be officer or enlisted man. From the evidence at hand, the odds are that he will have a recurrence on active duty. It is all very well to say that on our large ships there are able surgeons and ample facilities for handling ulcer emergencies, but we doubt whether the medical officer who treated the man in our series for massive hemorrhage at sea, while expecting contact with the enemy, would agree.

#### SUMMARY

1. The statistics on peptic ulcer from the Annual Reports of the Surgeon General, U. S. Navy, from 1917 to 1940 are reviewed and discussed.

2. Twenty-seven cases of peptic ulcer that were discharged from the U. S. Naval Hospital, Philadelphia, Pa., during the eight months ending September 30, 1942, are analyzed.

3. The question of disposition of the ulcer patient in military life is presented with points of view from various observers of the problem.

4. The authors conclude that no naval officer or enlisted man suffering from peptic ulcer should be discharged to duty without the recommendation of a Board of Medical Survey (subject to the approval of the Bureau of Medicine and Surgery). It is also stated that the Board of Medical Survey should recommend for return to duty, only those patients who are most indispensable and whose case histories are most innocuous.

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## MILITARY NEUROPSYCHIATRY IN THE PRESENT WAR \*

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### I

MILITARY medicine reflects both the military operations of the period considered and the current stage of medical advance. Each war has presented its own peculiar medical problems, some of which were not solved until after hostilities had ceased, some of which were solved brilliantly during the heat of battle, and others of which still remain. The scurvy of Washington's troops, the dysentery of both armies in 1861-1865, the typhoid of 1898, and the influenza of 1918 are as identifying in military medicine as are the tactics of the campaigns in which these medical problems arose. If one considers only the official reports of these wars, psychiatric problems either did not exist or were inconsequential in the American Armies until 1917. Actually, of course, these disorders did occur, were occasionally recognized and rarely reported.

As early as 1856<sup>1</sup> there were enough psychotic American soldiers, sailors, and marines to warrant the founding of what is now known as St. Elizabeth's Hospital in Washington, D. C. Psychiatric disorders, however, were not a military problem in any army until the Russo-Japanese War when the Russians first reported large numbers of mental disorders, particularly among the officer personnel engaged in that brief war.<sup>2</sup> The Japanese reported none. The German Army, prior to 1914, recognized such disorders and characteristic Teutonic studies were begun. The Surgeons General of the U. S. Army and the U. S. Navy started postgraduate study in psychiatry for medical officers at St. Elizabeth's Hospital in 1909.<sup>3</sup> The late Dr. W. A. White, then Superintendent of that institution, may well be considered the father of military psychiatry in this country. Kay,<sup>4</sup> studying the British Army in 1912, found, apparently to his surprise, that mental disorders were present in a significant number even during times of peace. He summarized his studies in what was then a satisfactory statement, "Insanity is invariably increased as a result of war." King,<sup>5</sup> in 1914, reviewed the neuropsychiatric state of the U. S. Army and made several observations which were, unfortunately, lost sight of in the war which followed three years later.

World War I, that dress rehearsal for today's conflict, brought functional nervous disorders into prominence as a by-product of war. Sutton<sup>6</sup> has expressed the belief that psychiatry made its first post-Kraepelinian prog-

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ress with the stimulus of the World War I case load. Whether one can consider this huge case load with its accompanying social and economic results as beneficial or not is beyond the scope of this presentation. It is clear, however, that more attention was directed upon disorders of the central nervous system, both functional and organic, during and after the first World War than previously.

That unfortunate term, "shell shock," made its appearance in both lay and medical literature during this period. One wonders if psychiatry, and military psychiatry in particular, will ever live down this expression. Many of the most prominent observers of that day subscribed to compression, air pressure, high explosives and similar bizarre etiological explanations for cases which were, in civil life, recognized as clear-cut psychoneurotic reactions.<sup>6</sup> Hurst,<sup>7</sup> Osler,<sup>8</sup> and others of equal ability subscribed to this then popular explanation.

## II

The Boer War was characterized by depression states.<sup>4</sup> The Russo-Japanese War<sup>2</sup> was characterized by alcoholic reactions, confusion states and gross hysterias. My associates and I have been interested in observing the incidence and characteristics of the neuropsychiatric disorders we have encountered in the U. S. Army during the present war. We can present at this time only a preliminary report based upon study of our first 200 cases. These data permit an indication rather than a final determination. These cases are shown in table 1. It is evident that more than 70 per cent of our cases fall into one of the following four groups: neuroses, psychoses, organic neurological or psychopathic personality disorders.

TABLE I  
Military Neuropsychiatric Admission

	No.	Per cent
Neuroses .....	43	22
Psychoses .....	37	18
Neurological .....	35	17
Psychopaths .....	28	14
Miscellaneous .....	13	7
No NP disease .....	13	7
No disease .....	10	5
Mental deficiency .....	9	4
Epilepsy .....	7	3
Alcoholism .....	5	3
Total .....	200	100

*Neuroses.* We have observed the usual varieties of psychoneuroses in this group but the most common neurotic reaction occurring here is that characterized by anxiety, depression, agitation, apprehension, suicidal drive, loss of energy, mental retardation, confusion, indecisiveness, insomnia and uncontrollable weeping. Table 2 shows the incidence of these findings in 20 cases of this series. Anxiety was present in each case as was depression. Eleven of the 20 cases were regarded as markedly suicidal. Three had made

suicidal attempts prior to arriving at the hospital, one by firing his service automatic into his left chest, another by leaping into a fire, and the third by cutting his wrist. This group was further of significance in that 18 of the 20 were officers and the other two were non-commissioned officers. Three

TABLE II  
Anxiety-Depression Neuroses

No. of Cases	No.	Per cent
Symptom	20	100
Anxiety	20	100
Depression	20	100
Retardation	20	100
Loss of energy	20	100
Apprehension	18	90
Suicidal drive	11	55
Confusion	10	50

were medical officers, three were chaplains and the remainder were from various arms and branches of the service. Physical examination and comprehensive laboratory and special examination survey procedures revealed nothing of clinical significance in any of these cases. The mean age of this group was approximately 34 years. This is 10 years greater than the mean age of the entire series. Longitudinal life histories and personality studies on this group of cases showed underlying personalities uniformly characterized by meticulousness, inadequacies, perfectionism and dependence upon others for the most trivial of life decisions. In each case of this group, the onset of the syndrome was relatively rapid, rarely extending over three weeks and, under therapy, recovery has been almost as dramatic. It should be noted that relief from active military duty has been a therapeutic as well as an administrative procedure in each of these cases.

*Psychoses.* The psychoses observed in this series have been predominantly schizophrenic in nature. These reactions have been most frequently encountered in young soldiers whose military service has varied from one day to three months. Schizophrenia, like measles, is a disease of recruits. Of the 37 psychotic patients studied in this series, 33 were schizophrenics. This group is shown in table 3. It will be noted that 10 of these cases

TABLE III  
Schizophrenia

No. of Cases	No.	Per cent
Ill prior to Army service	33	100
Previously committed	10	31
Previous shock therapy	7	21
Acute Schizoids	4	12
Schizophrenic (chronic)	11	33
	22	67

had been known to the family as mentally ill prior to entrance into the military service. Of these 10 cases, seven had been previously committed to institutions for mental care and treatment. Four of the previously com-

mitted cases had been discharged from other hospitals as "recovered" following the use of one of the varieties of shock therapy.

Eleven of these cases presented an acute schizophrenic illness characterized by withdrawal, negativism, mutism, autistic thinking, severe mental confusion, preoccupation, paranoid delusional content, accusatory auditory hallucinatory experiences, affective impoverishment and loss of insight. The underlying personality in these cases was characterized by sensitiveness, shyness, lack of self-confidence, deficient sex drive and immaturity. Under a rather simple regimen of protection, reassurance and graduated activity, all of this group recovered from the acute episode. These cases, too, were discharged from the military service for both therapeutic and administrative reasons. One of these cases was a young officer; the remainder were privates. The mean age of the schizophrenic group was approximately 24 years as was that of the smaller group who made rapid recoveries and of the total series of both neurological and psychiatric cases.

*Organic-Neurological.* In this group the traumatic cases predominate as a medical reflection of military mechanization. These cases are not battle injuries but represent truck, tank, automobile and airplane accidents. A smaller number of this group are peripheral neuritic syndromes such as Bell's palsy and toxic neuritides following a variety of causative agents. In the combat zone the organic, particularly the traumatic, group would be considerably larger and, with accelerated war preparation, may increase in the zone of the interior.

*Psychopathic Personality Disorders.* This group of unpleasant cases is present in our series in about the usual incidence rate of peace time. Study of this group has shown us nothing peculiar to the present war period.

### III

We have studied neuropsychiatric cases occurring in the U. S. Army during a mobilization and a war period. None of our cases is from the combat zone. The psychic stresses to which our patients have been subjected have been: (1) separation from home, familiar environs and the personal reassurance of the family; (2) strange occupations; (3) large responsibilities (in the case of officers); (4) fatigue; (5) impersonality of environment; (6) regulation of activities with loss of personal liberties; (7) strict accountability; and (8) anticipation of personal injury or death. These are the basic stresses of the military recruit in any period. The personality who was meticulous, perfectionistic, dependent upon others for constant reassurance and personal guidance could only develop an anxiety state when subjected to the radical change from his civil niche to military life. The Swiss Army mobilized during World War I developed this syndrome without firing a round.<sup>9</sup> The German Army has had this same problem<sup>10</sup> and undoubtedly still does, although no information is now available on the point.

The British Army has divided its military psychiatry in the present war into the pre-Dunkirk and the post-Dunkirk periods.<sup>11</sup> In the earlier period, mental deficiencies, epileptics and anxieties predominated. With Dunkirk, however, exhaustion deliria and acute confusion states prevailed. The Canadian Army studied by Baillie<sup>12</sup> showed, in the earlier stages of this war, a preponderance of psychopathic personalities, mental deficiencies, organic cases and epilepsy. His series showed a low incidence rate of neuroses and psychoses. Baillie's data are comparable to ours in that he studied 200 cases in the Canadian Army preparation period of the war. The Canadian, according to some observers,<sup>13</sup> has presented more psychosomatic manifestations than has the U. S. Army group. The exact cause for these differences is not evident at this time.

In the cases which we have studied, the psychoneurotic syndrome of anxiety with depression has predominated as the neurosis of this war. The psychodynamics of this syndrome appear, upon the preliminary data now available to us, to be essentially that of an insecure, worrying perfectionistic personality placed in a position of what is, to him, intolerable stress with resultant anxiety, depression, retardation and related symptoms.

Schizophrenia is the psychosis of major military significance now as it has been since the disorder was first recognized. In the U. S. Army of peace time, this disorder is approximately three times as common as it is in the comparable age and sex group in civil life.<sup>14</sup> This phenomenon has been studied several years by various workers. Hoffman, Parsons and Hagan<sup>15</sup> reported a 12 year follow-up study of these cases with findings which indicate less chronicity of this disorder among military personnel than among young men in civil life. Duval and Hoffman continued these studies observing that acute schizophrenic episodes with rapid onset and early recovery occurred in 47 per cent of their military cases. Anderson<sup>17</sup> is engaged in a similar study of these cases and suggests that they are not schizophrenia in the usual or dementia praecox concept. The syndrome is clearly a psychologic escape mechanism which occurs in shy, timid, immature young men inducted into the military service or enlisted for the misguided purpose of "being made a man of."

We have not utilized shock therapy in the treatment of schizophrenia. Twelve per cent of our cases had previously "recovered" after treatment by this method. One-third of our cases have made what appears to be complete recoveries at the end of relatively brief hospitalization, and an additional one-third were markedly improved. In our practice, therefore, shock therapy appears unwarranted.

Neurological disorders are, in the military service, predominantly traumatic in origin. Disseminated sclerosis, however, is not infrequently encountered as are a few brain tumors and a considerable number of peripheral neuritides. An increasing number of traumatic neurological cases is expected with accelerated training of mechanized forces and battle casualties.



The psychopathic personality is a constant military as well as civil problem. Cleckley<sup>18</sup> has recently reviewed this problem in a most comprehensive manner. Porter,<sup>19</sup> Parsons, Ewalt and Peake, and Hall<sup>20</sup> have presented the military inaptitude of this group. There is a unanimity of opinion that these individuals cannot be utilized in any part of the military service. We feel that they cannot be treated, and we present no medical solution to this most important psychiatric problem today.

#### IV

Our preliminary report deals with 200 military neuropsychiatric cases hospitalized during the period of preparation and early months of the present war. We find that the characteristic neurosis of this period is anxiety with depression. The psychosis is schizophrenic in nature with one-third of the cases presenting acute episodes which subside quickly. Traumatic neurological disorders have been prominent in our cases, and we anticipate increasing prominence.

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## PSYCHONEUROSES IN WAR TIME\*

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IN the Dialogues of Plato, written more than 2000 years ago, one finds the following description of Herodicus:

"He had a mortal disease which he perpetually tended, and as recovery was out of the question, he passed his entire life as a valetudinarian; he could do nothing but attend upon himself, and was in constant torment whenever he departed in anything from his usual regimen, and so dying hard, by the help of science, he struggled on to an old age, a rare reward of his skill!"

This description suggests to us that the disorders of human nature have not changed much since ancient times. No modern diagnostic term, such as psychoneurosis, can do better than such a descriptive paragraph.

Internists and surgeons, finding no disease of the body in disabled and complaining patients, are inclined to call the disorder a psychoneurosis. The psychiatrist does not arrive at his conclusion in this negative way. He has in mind a positive syndrome that may be deduced, not from the physical examination findings, but from the qualities of human nature observed. We shall go more thoroughly into these aspects of persons a little later, to see what groups or reaction types we may find.

One of our most vital qualities is the energy we possess, especially energy for doing useful work. The work record of patients is extremely important. How much can he do? How dependable is he? How consistently does he work? During the last World War the Germans did not use the word "psychoneurosis," but designated its counterpart as describing persons not overtly psychotic and with a *lowered threshold for useful work*.

Perhaps another way of saying this is that each person is endowed with a given amount of something we may call adaptability. It wears out, as life itself does. Those of our men and women between 18 and 45, or over, who have been entrenched in civilian life and have adapted to it, will have to readapt to the regimentation of military life, to heat, cold, high altitude, and to effects of the desert or the jungle, to say nothing of the enemy. When the war is over, they will be required to readapt again to a changed civilian world and do it with changed selves. The strain on adaptability is likely to result in some breakdowns that will require tolerance and understanding.

In World War I it was said that no new types of psychosis or neurosis were seen which were not found in civilian life. That was true and is essentially true today. Aviators who fly too much are said to become stale, bored, and irritable. Long-continued use of noisy mechanized equipment is a strain on attention and other functions as well. The very necessary and

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circumscribed regulations of naval men, especially while at sea, result in some breakdowns that may be peculiar to their work. The fact seems to be that anyone will break down if the stress, by virtue of its quality or degree, becomes great enough, and some persons will do so when the external stress is hardly perceptible. Gillespie<sup>1</sup> (Psychiatrist-in-Chief, for the Royal Air Force) has reported relatively little increase in the incidence of neuroses from the bombings in England unless there was predisposition. These latter conditions are a problem for induction boards which are doing a much better job in this war than they did in the last. Their work cannot be perfect because of latent subclinical tendencies in all of us.

Let us review briefly some of the types of neurosis likely to be encountered but first present a disorder that is common enough although not really a psychoneurosis.

*Unstable States, or Reactions to Situations.* Often in life a person must make a difficult decision, or must face distressing facts and he may, as a result, become tense, tremorous, sleepless and emotional. Such conditions sometimes produce symptoms requiring the help of a physician. Patients not infrequently have headaches, or vomit, or ache under such stress. An opportunity to talk it over with an understanding friend, or clergyman, together with the relief of individual symptoms, is very helpful in such cases. Physicians occasionally make the mistake of giving the patient a list of serious diseases they have ruled out by their examinations, before concluding that matters are not serious. Quiet assurance and sound sleep are very therapeutic in such situations. Telling a patient that "it is all in your head" may lead to worse things. There are plenty of such mild disorders on every medical or surgical ward. Such patients appreciate reassurance and friendly advice; let us hope that the physician may not be so preoccupied with science that he fails to lend this human touch. These disorders have the same relation to psychiatry that the common cold has to infectious diseases; they are not very unusual, and often pass over quickly. An aviator flying too much, a soldier at the front too long, a sailor at sea too continuously, may show a little of such reactions. Such seemingly trivial and reversible disorders may have very strategic importance. An aviator may crash because of it. A gunner may miss his mark. A colonel or general may conceive or execute the wrong plan. Change, rest, relief, understanding are very therapeutic, although vigorous men may feel that they are indulging themselves when placed on such a regimen for even brief periods.

Now, let us turn to the disorders that are commonly called psychoneurosis; a word, I fear, used too glibly to dismiss an undesirable patient and to discharge a responsibility that does not really end when the diagnostic term is applied.

1. *Hysteria—Substitution Disorders.* The disorder, hysteria, was first singled out by the ancients who believed that certain cries and distresses of women were in some way related to malpositions of the uterus, the word for uterus in Greek being *hysteros*. Not until the 17th century did the con-

cept change to include men, and then, of course, it became certain that it was not due to the uterus. The word "hysteria," however, lingers with us as a relic of false and ancient concepts. The term has wide use among laymen and refers to undue laughing or weeping, or emotional instability; for example, "crowd hysteria, hysterical with laughter, hysterical over bad news." A better term is substitution disorder, or sublimation disorder. Freud has contributed the chemical concept of sublimation, which is this: that emotions may not appear as such, but may appear instead as body disorders, or a deletion of body functions. There is a certain amount of *mimicry* about this. Butterflies mimic; so do rabbits; chameleons depend on mimicry for almost all of their protection. Why shouldn't man occasionally be so constituted that in the face of stress he unknowingly imitates disorders that he has seen, such as blindness, paralysis, aphonia, pain, gait disorders, forgetfulness, confusion, syncope, etc. These substitutions of body symptoms and personal behavior for the emotions growing out of stress are really pseudo-symptoms and are recoverable under the influence of suggestion, hypnosis, anesthesia, various types of narcotization, by establishing a penalty for retaining them, and rewarding by pleasure for giving them up. Faradic electricity judiciously used may help to accomplish this.

After the gross symptoms have been overcome, the patient's life needs to be organized so that unendurable stress is removed, and he is rewarded for remaining a useful citizen. All of these things must be done, not with the feeling that the patient is malingering, but in the spirit of kindness and firmness and hopefulness. To tell such a patient that there is nothing the matter with him is to fail before beginning.

2. *Invalidism; Irritable Weakness Syndrome.* Between the years 1860-1870, Beard and Van Deusen used the word, "neurasthenia," as a diagnostic term for patients disabled by weakness, irritability, and disappointment. Their patients were chiefly society women, bored by the round of futilities to which people subject themselves. The word itself means "weak nerves," and as such is clearly a misnomer. In certain forms of leprosy and neuropathies, and neuritides, there really are damaged and weak-functioning sensory and motor nerves which are definite structures carrying impulses between the periphery of the body and the central nervous system. Then, too, there are so many diseases and conditions that can make people weak; for example, Addison's disease, myasthenia gravis, incipient Parkinsonism, tuberculosis of the lungs, melancholia, too much work, no chance to rest, etc. The diagnosis "neurasthenia" is being used and spoken of less and less, and in some excellent clinics it is never made. But constitutional asthenia, or constitutional inadequacy, or the more accurate descriptive terms, irritable weakness syndrome, or invalidism, are more understandable as a real *energy defect*. Persons with energy defects, born into families of accomplishment, seldom have recourse to honest appraisal of themselves. They are obliged to explain their condition in terms of illness, which is socially approved,

and never in terms of the variation from the average in energy, which it really is. This is illustrated by the history of "patient X" which follows.

#### CASE REPORT

"X," aged 34, complained of tiredness, weakness, mild insomnia, and some indigestion for at least 12 years. During childhood he had many colds and infections but none was serious. In preparatory school he was never strong enough to take an active part in sports and sometimes a tutor was needed to help him with his studies. He got on well with others. His father is a successful manufacturer; a younger brother is a college teacher; an older sister is an active club woman, the mother of two children. The family were disappointed when the patient was unable to go on with postgraduate studies—particularly the mother, quite a religious woman, who had hoped that her favorite son might enter a profession.

The patient had been examined by several physicians. The first told the family, "the physical examinations and laboratory tests are all negative; his trouble is *nothing but mental*." The family took offense at this. Another physician found no body disease, but felt that the endocrines might be "out of line" and so prescribed extract of adrenal cortex; for a while it seemed to help, but not enough to satisfy the ambition of the family. A third physician, noting that the patient maintained his weight with difficulty, wondered if he had received all of the vitamins he needed and accordingly these were prescribed. The patient gained weight temporarily, but was unable to do more effective work. These were only a few of the physicians who saw the patient. Some advised less pampering and even intimated that he was "giving in to himself." These diagnoses were made by various physicians: neurotic, neurasthenic, a plain case of nerves, chronic nervous exhaustion—apparently satisfying the physicians who made them, when in reality they should not, since "diagnosis" means "to know the disorder through and through" and merely attaching a word label is little better than classifying diseases by lottery. Against their own wishes, and at the suggestion of a physician, the parents finally took the patient to a psychiatrist whose examination of the body, including the nervous system, likewise proved negative. The family asked many questions and expressed the hope that the psychiatrist would find "X"'s trouble "merely nervous, and not mental." They were told that "X"'s body was in pretty good condition, but that *he as a person* was ill or disordered; that the disorder was of long standing and deep-seated—far more difficult to eradicate than some more striking conditions called mental. The psychiatrist informed them that "X" was very honest and sincere about his disability, never "putting it on" for the sake of escaping responsibility. He explained that if human beings were like machines or engines, cause and effect might be easily related; but, on the contrary, biologic evolution had created persons in whom cries of distress and evidences of disability were somewhat removed from the immediate apparent causes and might be symbols of something not quite obvious. The psychiatrist further explained that such patients are often very intelligent, but have *energy defects* that interfere with family and personal ambition. Charles Darwin, he told them, was such a person, accomplishing much with meager energies, although he was never quite at peace with himself or the world about him. An effort was made by the psychiatrist to adjust the patient honestly to a program compatible with his real assets; "X" was disappointed in this, and he knew his family would be. Later they sought the advice of a surgeon who focused on his indigestion, ignoring most of his other disabilities, and "X"'s appendix, not seriously diseased, was finally removed. The last news of "X" reported him to be devoting a part of each day to oil painting, reasonably contented with his accomplishments, but ever mindful of how he had been "cheated out of success in life by bad health."



There is no place for "X" to fit into the duties and responsibilities of the active military forces, which are not therapeutic agencies. Should "X," by accident or otherwise, get into the armed forces, the ultimate cost to the government in providing for him runs into thousands of dollars, according to the records of World War I.

3. *Psychasthenia—Compulsive-Obsessive Neurosis*. In 1903, Janet used the word psychasthenia as a diagnostic term for disorders characterized by "weak mind"—a literal translation of the word. By this, he did not mean feeble-mindedness, as the word might imply. He referred to those in whom indecision is a disability, and who are obsessively distressed and preoccupied with topics of an unusual nature, but with insight into their condition. Freud coined the more descriptive terms, compulsive-obsessive neurosis for such conditions. Individuals so affected are aware of the unreasonableness of their obsessions, and the absurdity of the compulsions, which are acts indulged in by the patient to bring relief for the obsessions. One of the commonest obsessions is a dread of dirt or filth. The compulsion indulged in to get relief is cleaning over and over again, or excessive hand washing, sometimes to the point of exhaustion. Other obsessions center in contamination fears, need for punctuality, for neatness and orderliness, "for saving one's soul," strange body feelings, fear of crowds, fear of diseases, etc. For relief from these obsessions, compulsions of meticulousness, scrupulosity, and frequent medical consultation and health precautions, or religious preoccupation, are often observed. Sometimes unusual rituals are followed. These patients adjust by an *uncontrolled and repetitious automaticity*. Alcoholic excesses are not infrequently on an obsessive-compulsive basis. Persons so disabled have unstable physiological equipment, and may vomit, have diarrhea, anorexia, and other symptoms, too, from the exhaustion created by repetition of compulsions.

The disorder occurs in two forms. One is insidious and has existed pretty much the whole life of the patient. This form is usually not responsive to therapy, and the most that can be expected, in our present state of knowledge, is to get the patient to adjust to some simple work that is not too demanding. The other form occurs in more or less circumscribed attacks. Such patients respond to treatment in much the same way that depressed or elated patients do, and tend to recover. Electroshock therapy may be of definite value with this group. Bilateral prefrontal lobotomy is said to be helpful.

4. *Anxiety Neurosis, or Anxiety States*. These disorders occur when the patient feels that his life, or his integrity, is threatened. Many persons whose lives are menaced by serious disease do not develop a panic, or fear of death. On the other hand, persons may allow their thoughts and feelings to build up a conviction that death is imminent if relief is not obtained. *Pathological self-preservative reactions* form the basis of this disorder. Such attacks punctuate an otherwise tense existence which may last several months to several years. These disorders are not easily changed by sug-

gestion or persuasion. Psychoanalysis is said to be helpful. They border on depression or melancholia, and may be responsive to sleep treatment, insulin to the point of inducing sleep, and even to electric shock therapy. Because of the disposition to have rapid pulse and perspire freely, the treatment must have especially close supervision. Many of these disorders are erroneously mistaken for toxic goiter. Mild sedation is desirable throughout the 24 hours to enable the patient to feel more secure. These patients are often suicidal and definite precautions should be taken to prevent it. They constitute in their variety by far the larger part of the psychoneuroses developing on the battle field.

5. *Hypochondriasis—Hypochondriacal States.* These disorders originally referred to the region under the costal cartilages (hypo-kondria); because other parts of the body may be implicated, the term is really another misnomer. To such patients the body rarely feels comfortable. The abdomen is distressing, the heart may feel heavy, the lungs may be suspected, the genitals may cause discomfort. Bizarre notions sometimes exist, such as "the blood drying up, the stomach rotting, the lungs filling up, the liver clogging, the heart losing its power, the face becoming distorted." Such patients declare that they would be well except for such varied and unpleasant feelings, and they go from one physician to another seeking relief. Personal disintegration takes the form of *body distress and discomfort*—not on a mimicry basis—but with *delusions about their cause*. They resemble paranoia in that they project their distress to the body, however, instead of to the environment. These patients are not weak and struggle to carry on. Hypochondriasis differs from invalidism in that these patients are more capable of working, part of the time at least. These disorders are doubtless closely related to some of the more overt psychoses, and are known for their chronicity and unresponsiveness to treatment. Fortunately they are rare.

6. *Traumatic, Post-traumatic, Post-concussion Neurosis.* It has long been known that a disabling syndrome may occur following severe trauma, or shock. It may take many forms, and change in mood, loss of energy, uncomfortable and distressing feelings are common. However, the mere fact that it does not occur in all cases of severe trauma, but merely in a few, gives strong proof to the theory that only certain persons are predisposed. Electroshock and metrazol shock have taught us many things. Chief of these is that shock drives the patient from one emotional state into another. This leads us to suspect that severe trauma or concussion, or the effect of violent blast, may dislocate the emotional integrity of otherwise well, but predisposed persons, to make them ill. This is really *modern shock treatment in reverse*. Such disorders heretofore called post-traumatic or post-concussion neuroses are usually affective disorders. A small percentage may fall into the group of neuroses previously described, especially in view of the fact that the possibility of compensation may add impetus to certain

forms of mimicry and defensiveness. The physiological and anatomical effects which may result from violent trauma and blast are not adequately understood and constitute a fertile field for research. For these reasons, post-traumatic or post-concussion neurosis may be misnomers which, as we have seen, have been so prevalent in the nomenclature of psychoneuroses.

*Treatment* of the psychoneuroses must be individual, but should be planned so that we do not expect more of the patient than he can honestly deliver. For those whose adaptability has become strained or bankrupt, let us provide therapeutic facilities of all types, hopefully, and for a reasonable time. Psychoanalysis takes too long for more than a few patients, although some shorter modifications of it may be useful. Insulin may be employed to induce sleep, or a better state of nutrition. Electric shock may be very helpful on occasion. Mild sedation, graduated exercise, physiotherapy, occupational therapy, recreational activities, psychotherapy—teaching the patient to live within his capacities, to divorce himself from inflated ambitions—all of these will help the psychoneurotic to utilize his assets and to feel his defects and disabilities less painfully. Treatment, except in the hands of the experienced, causes these patients to seek help far and wide, in and out of the medical profession.

The word "psychoneurosis" has many meanings to different people. It is not a condemnatory term, but should conjure up a descriptive picture: that of a person disabled in any one of the several quite specific ways I have previously sketched. It is not a negative entity; it is really a very positive one. It is rarely pure: combinations exist, one of the chief being depression, with neurotic tendencies. Whether the disorder is a mild psychosis or a neurosis is often the source of fruitless academic argument. One thing seems certain; such patients appeal to the internists and surgeons repeatedly for help before they finally come to the psychiatrist. They may accumulate a collection of surgical scars in their quest for relief. All too frequently they are treated as time-consuming intruders because of the paucity of physical findings. The psychoneurotic is, of course, subject to all the diseases of the body that can attack anyone else, and may even become psychotic.

Psychoneurotics, except for the severer but rarer forms encountered on the battlefield, are not completely disabled. They carry on by fits and starts, seasonably and sporadically, often compensating for energy defects by engaging in intellectual pursuits. I know one whose specialized judgment in the financial world enabled him, in a brief period, to make a large sum of money while in bed with his disability. The psychoneurotic is sensitive and often makes up for quantity by the quality of his work. He is included among the artists and the aesthetic. In spite of his disabilities, we are indebted to him for contributing to a more refined world in which to live, and he needs what help we can bring to him.

War does not cause psychoneurosis, except as the predisposed are broken down by it. War requires strenuous, continuous effort, often in the presence of unspeakable horrors. It is a race for the strong and the tough, and

psychoneurotics should be rejected for active military duty when recognized as such.

#### SUMMARY

1. Absence of body disease is not a criterion for diagnosis of psychoneurosis. Psychoneuroses may have any of the body diseases that others have. They need the usual physical and laboratory examinations. The diagnosis is based on the positive way a particular kind of predisposed human nature adjusts. The relatively unpredisposed may develop a variety of symptoms resembling those of the psychoneurotic if under sufficient stress. These symptoms usually disappear quickly when the stress is relieved.

2. Substitution disorders (hysteria)\* are based on *mimicry* found abundantly in plants and animals.

3. Invalidism (neurasthenia) is a way of adapting when there is a pronounced *energy defect* in a person goaded by ambition.

4. Compulsive-obsessive neurosis (psychasthenia) has its inception in a disposition to *uncontrolled and repetitious automaticity* of feelings and acts, which are also widespread among the animals of nature.

5. Anxiety neurosis is the adaptation of a person with *pathological self-preservative impulses and reactions*—the neurosis more intimately associated with the battlefield than any other.

6. (Hypochondriacal disorders) are forms of adaptation on the part of those with more or less personal disintegration in the nature of persistent delusions about the shape or functions of their bodies. These disorders tend to be chronic and are hardly to be distinguished from chronic psychotic states.

7. So-called (post-traumatic and post-concussion neuroses) are, with some exceptions, *affective disorders*, which may result from trauma: shock effects in reverse, so to speak.

8. Many psychoneurotics respond to the various forms of therapy that are available. Treatment must be very individual. Despite their disability, many of them make a definite contribution to our culture, but are unfitted for active military service.

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\* Misnomers are in parentheses.

## THE TREATMENT OF FUNCTIONAL GASTRO- INTESTINAL DISTURBANCES OF NEURO- PSYCHIATRIC ORIGIN \*

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### INTRODUCTION

THE gastrointestinal tract is particularly susceptible to functional disorders characterized by physiological abnormalities in the motor, secretory and sensory spheres, not due to any known primary structural or chemical causes, deficiency states or allergic disturbances, and traceable to neuro-psychiatric maladjustments. These cases are frequent in everybody's practice and are usually unsatisfactory from the standpoint of treatment. It is the purpose of this presentation to discuss treatment, but before doing so it is necessary to get some clear formulations of the rôle of the vegetative nervous system and more particularly some principles in general psychopathology of the psychoses and neuroses, and some special psychopathology of the psychoneuroses. Without these formulations no principles of treatment can be formed.

*The Rôle of the Vegetative Nervous System.* The common denominator of all disorders of the gastrointestinal tract, either organic or functional, is the physiological disturbances in the various functions of the vegetative nervous system. The vegetative nervous system is the "great common path" in the various motor, secretory and sensory disturbances of this tract.

For practical purposes, the vegetative apparatus may be divided into three parts:

1. The autonomous structures comprised by the myenteric plexus of Auerbach and the submucous plexus of Meissner which, though autonomous, are markedly influenced by the two major divisions of the vegetative nervous system.

2. The two major divisions of the nervous system, the sympathetic (thoracolumbar) and the parasympathetic (craniosacral) systems. It is important to stress that both of these systems contain both efferent and afferent pathways.

3. The suprasegmental connections, also a two way system of which the *diencephalon* is probably the most important constituent. Experimental and clinical evidence suggests that the *diencephalon* plays a major rôle in regulating efferent impulses of both divisions of the vegetative nervous system. It is worth stressing that the *diencephalon* now is recognized as having a

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marked influence upon the endocrine glands, metabolism and heat regulation, as well as receiving impulses from and sending them to the old and new brain and the neuraxis. Even more important is the fact that the region of the diencephalon is regarded as one of the major centers of emotions.

Little is known about the cortical representation of the efferent vegetative nervous system, but Fulton<sup>1</sup> states that such representation exists in the premotor area (Broadman Area VI).

The reader is referred to appropriate literature for a detailed discussion on the anatomy and physiology of the vegetative nervous system. Of particular interest to the clinician is the cause of pain arising from the viscera.

At one time it was thought that there were no sensory nerves in the viscera, especially in the gastrointestinal tract, and that pain was always a result of the involvement of the structures supplied by the somatic nerves, such as the parietal peritoneum.<sup>2</sup> Later it was agreed that pain occurs in disturbances of the gastrointestinal tract by overdilatation<sup>3</sup> and overcontraction<sup>4</sup> of hollow viscera and by stretching of the capsules of the solid organs. Still later Ross,<sup>5</sup> Head,<sup>6</sup> and MacKenzie<sup>7</sup> evolved the concepts of viscerocutaneous, visceromotor, and viscerovisceral reflexes to explain the various painful phenomena originating in disease of the internal organs. More recently Leriche<sup>8</sup> pointed out that the viscera have sense organs identical with those in the skin, but they are subjected only to intrinsic stimuli which, even if they reach consciousness, are not and cannot be interpreted in terms of other analytical data.

Recent experimental and clinical observations have led to the impression that the diencephalon plays a major rôle in the disturbance of the gastrointestinal tract both from physiological and emotional standpoints since the diencephalon is a relay station for fibers mediating a great many functions including the emotions.

When one bears in mind the physiology of the involuntary nervous system it becomes easier to understand why the gastrointestinal tract can become a prey to conditioned reflexes. This is particularly true early in life in relation to appetite, vomiting, constipation, diarrhea and other disturbances of the gastrointestinal tract. It is important to stress that these gastrointestinal disorders are not simple reflexes but rather, physiological reactions having their origin in complicated psychological situations.

*General Psychopathology.* The special psychopathology of the neuroses will be considered under the treatment of the neuroses. Here it is desired to state that every clinician, for purposes of treatment, should have some knowledge of the structure of personality, types of personality and reaction types.

*Structure of Personality.* *Personality* may be defined as the sum total of all reactions in a given individual. It includes the habitual patterns of behavior of the individual in terms of physical and mental activities and attitudes (Healy, Browner, and Bowers).<sup>9</sup> A fundamental, empirical, but necessary concept of personality necessitates the division of the personality

into two parts: unconscious and conscious. The unconscious monopolizes the greater part of personality. It has often been compared with the submerged part of an iceberg, the visible part representing the conscious. The unconscious is defined as a deep level of mental activity consisting of elements which never were conscious (collective unconscious of Jung<sup>10</sup>) and of elements previously in consciousness but forgotten, suppressed or repressed. *Suppression* is a purposive exclusion of ideas from the field of conscious attention. *Repression* is an unconscious exclusion of painful and unpleasant material from consciousness and from motor expression. Repression is directly or indirectly accomplished by that part of the personality which is concerned with the adaptation of the individual to the needs of reality. The unconscious is brought into consciousness only in dreams, abnormal states, and by special psychological technic. The conscious part of the personality is at all times markedly influenced by its larger unconscious part.

*Types of Personality.* From a clinical standpoint personalities may be divided into the following groups: (a) average normal, (b) neurotic: hysterical, hypochondriacal, oversensitive, compulsive-obsessive, (c) syntonik (cyclloid, extraverted), (d) schizoid (shut-in, introverted), (e) paranoid, (f) rigid, (g) constitutional psychopathic, (h) epileptic.

*Reaction Types:* From the standpoint of psychopathology it is well to be familiar with the several reaction types. These include:

(a) the *organic reaction type*, such as occurs in structural diseases of the brain due to vascular and degenerative changes, neoplasms, infections, intoxications, deficiency states, and characterized by predominantly intellectual difficulties;

(b) the *affective reaction type* comprising principally the cyclic manic-depressive reactions and involutional melancholia;

(c) *Schizophrenic reaction type* with the many bizarre modes of thinking, feeling and acting observed in various types of dementia praecox, and

(d) the *psychoneurotic reaction type* which will be discussed in detail later.

Functional gastrointestinal disturbances are observed with varying frequency in the various types of reactions. The etiological diagnosis depends, in a large measure, on evaluating the type of personality and reaction, and without such an evaluation treatment is unsatisfactory. It is important to emphasize that it is not the gastrointestinal disturbance that makes for the useful diagnosis, but the setting in which it occurs; that is, the evaluation of the associated clinical phenomena.

For practical purposes the treatment of the various gastrointestinal disturbances will be described first from the standpoint of their occurrence in the various psychotic reactions, and then in the psychoneurotic reactions.

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Only the more frequent gastrointestinal disturbances will be touched upon in this presentation.

*Bitter Taste in Mouth.* This is almost a constant complaint in depressions, even in the so-called extramural depressions which are often misdiagnosed and treated for colitis (Yaskin<sup>11</sup>).

*Anorexia* is a constant and prominent symptom in almost all depressions. Some depressed patients complain that they feel hungry but can not eat, that everything tastes alike or is tasteless. Many depressed patients have no appetite in the morning, but can tolerate or even enjoy a meal in the latter part of the day. With the onset of recovery the appetite for meals in the earlier part of the day improves.

Failure to eat is frequently observed in schizophrenia where it may be due to apathy, lack of interest, catatonic negativism or delusional states.

Anorexia is a common symptom in organic psychotic reactions.

*Bulimia* or excessive appetite is observed in some feeble-minded, in paretics and senile demented, and in some schizophrenics. The latter also evince a tendency to swallow all kinds of things, even their own excrement (coprophagia).

Picae, or peculiar cravings for food, are rare in psychoses.

*Alternating anorexia and bulimia* are often observed in early and borderline schizophrenia, sometimes accompanied by diet ceremonials. These phenomena usually represent morbid impulses (actions carried out without reflection and aimful willing), but may be due to delusional trends.

*Pain, paresthesias and dysesthesias referable to the upper digestive tract, abdomen and rectal region* are common in constitutional psychoses and require careful evaluation. They may occur as early and monosymptomatic manifestations in dementia precox and especially in involution melancholia. Indeed, in the latter disease, they may receive considerable attention from the organically minded internist who fails to observe the associated personality disturbances. Many useless investigations and operations are performed before the patient shows the more fundamental evidences of agitated depression and anxiety.

*Salivary, gastric, biliary, and pancreatic secretions* show some changes in the various psychoses.<sup>12</sup>

*Cardiospasm* is rare in psychoses, but vague complaints of difficulty in swallowing are fairly common early manifestations of involution melancholia.

Gastric and intestinal *motility* is disturbed in most of the psychoses.<sup>13</sup>

*Constipation* is a common manifestation of most psychoses, but especially the depressions. Fecal impactions are frequently found in psychotics. The depressed patient fails to move his bowels because of atony, psychomotor retardation or delusional states. In the schizophrenic retention of the feces

is observed in catatonic negativism, in delusional states, and most commonly due to apathy and inattention.

*Vomiting* is rarely seen in schizophrenia but is not uncommon in the tubefed depressed patient who makes every effort to terminate his life.

*Hypochondriacal and nihilistic* delusions such as those in which the patient is convinced that his bowels are obstructed and that the stomach is cancerous, are most common in involution melancholia, but may be seen in the early stages of dementia precox. The psychopathology of these delusions is interesting.

In reviewing the various gastrointestinal disturbances encountered in the psychoses one readily observes that the same manifestations may occur in the several types of reactions. It seems that the psychotic disturbances are reflected in changes of secretion, motility and sensation at the vegetative-visceral level, but in addition, misinterpretations and elaborations at the psychic level occur, resulting in hallucinatory and delusional formations. The early recognition of the underlying etiological psychotic process is of more than academic importance. With recent advances in the treatment of the psychoses, especially manic-depressive and involution melancholia, in which gastrointestinal complaints are early and prominent symptoms, a timely diagnosis means not only shortening the time of suffering and prevention of suicide, but effective immediate treatment. In schizophrenia the advances in treatment are less spectacular, but there are those who believe that early insulin shock therapy, plus psychotherapy, result in some recoveries, in many arrests of the disease, and in some improvement.

In turning our attention to functional gastrointestinal disturbances, as observed in the neuroses and psychoneuroses, we must utilize an entirely different approach if we are to be therapeutically successful.

#### TREATMENT OF THE FUNCTIONAL GASTROINTESTINAL DISTURBANCES IN PSYCHONEUROTIC REACTIONS

Every experienced internist is aware that the gastrointestinal disturbances occurring in the neuroses do not differ widely from other disturbances in the same disease. Furthermore, it is generally recognized that the treatment of the neuroses is often difficult and frequently unsatisfactory in the hands of the general practitioner, internist and others not specifically interested in neuropsychiatry. The reasons for these difficulties arise from failure to appreciate the importance of a number of factors, some of which it is my purpose to discuss. These factors include:

1. Failure to possess a minimum knowledge of the psychopathology of the neuroses.
2. Faulty attitude of the physician to the problems of diagnosis and treatment.
3. Lack of a thorough knowledge of a few principles in therapy.



*Some Basic Principles of the Psychopathology of the Neuroses.* The psychoneuroses and neuroses may be defined as conditions characterized by a variety of subjective complaints without any primary structural or chemical causes to account for their existence and generally traceable to some disturbance in the psychological processes of the individual. In the psychoneuroses the causative factors are traceable to occurrences and phantasies of early life with reactions to these incidents in the form of personality traits. In the neuroses the causative factors are traceable to occurrences or situations in the recent past or immediate present. In this presentation the terms "neuroses and psychoneuroses" will be referred to as "neuroses."

There is no gross or microscopic morbid anatomy or chemical aberrations to guide the physician in the diagnosis and therapy of the neuroses. Yet neuroses, like other natural phenomena, must have a beginning, an evolution and some reason for the various manifestations. This is to be found in certain psychopathological formulations, not all of which stand the tests of scientific criteria. Thus the concept of "personality" itself is, for the most part, a philosophic abstraction, but one without which treatment of the neuroses is hardly possible. The personality as previously stated is the sum total of all reactions experienced by an individual. From the standpoint of the neuroses the most important aspect of the personality is the *emotional* (affective) reaction. These emotional reactions may have their origin in situations of which the patient is perfectly aware (in the conscious) or (in the unconscious) in occurrences or phantasies of the past of which he is totally unaware. The existence of the unconscious has not been proved but, at present, it is a necessary hypothesis in the management of the neuroses. The unconscious activities of the personality are comparable to the activities of most of the thoracic and abdominal viscera of which we are not normally aware but which, nevertheless, exert a determining influence on our very lives. It is only when the viscera become disturbed that we become *aware* of them by reason of symbols which we call symptoms. Symptoms in organic medicine are often clever disguises, as edema in Bright's disease, glycosuria in pancreatic disease, etc. It has taken thousands of years to correlate the bizarre symbols with their true causes. This tendency for nature to disguise and symbolize is even more marked in psychopathology and makes the subject at times very complex, but, just as in organic medicine, there is always a chain of events to account for the occurrence of the various phenomena. Most of us can understand the occurrence of tachycardia, vomiting, diarrhea or fainting as an *immediate* result of some great emotional shock as easily as we understand the vomiting in obstruction of the gastrointestinal tract or the tachycardia in the failing heart. Some may doubt that insomnia, abnormal fatigability and irritability, phobias and many visceral disturbances are entirely due to emotional disturbances which occurred years before the development of the symptoms, although none of us *at present* questions that tabes and other marked changes in the various organs had their origin in a humble small cutaneous lesion called a



chance. It is a fact, nevertheless, that many neurotic symptoms are prolongations of early emotional states which remain dormant in the unconscious part of our personalities until some exciting cause activates them.

The concept of the neuroses as a distinct clinical entity is necessary for diagnosis and especially for successful treatment. In actual practice, however, it is frequently difficult to distinguish between what is "neurotic" and what is "organic." This is due to the fact that every disease must be considered as having both a somatic and a psychic component. The two components are indivisible and should be evaluated in their relation to etiology and to the total situation (Weisenberg, Yaskin, and Pleasants<sup>14</sup>). Whether the disease arises as a result of structural changes in the soma, of abnormal chemisms, or of emotional conflicts or abnormal psychic tensions, a change of affect of the individual (the subjective phase) and corresponding changes in the neuromuscular, autonomic, and secretory functions (objective evidences-emotional expression) takes place. As stated previously the principal relay station for emotional components of diseases appears to be in the diencephalon. It is responsible for the correlation of psychic and somatic disorders, has a regulating influence upon both of the major divisions of the vegetative nervous system and indirectly upon most of the endocrine glands, upon metabolism, and heat regulation. It also receives impulses from, and sends impulses to, the old and new brain and the neuraxis. In primary somatic disease this center receives abnormal impulses and registers them in the viscera in the form of emotions, especially in the abdomen, the "sounding boards of emotions" (James<sup>15</sup>). In disorders of the general chemism the center may be affected directly or centripetally via the vegetative nervous system. In states of emotional conflict and abnormal tension this center may be influenced from the cerebral cortex and then set up impulses responsible for secondary changes in function and even in structure of the viscera (Alvarez,<sup>16</sup> Moschowitz,<sup>17</sup> Weiss<sup>18</sup>). A consideration of these factors requires as criteria for the diagnosis of a neurosis not only the absence of any primary physical or chemical changes, but more particularly the finding of satisfactory psychological causes to account for the clinical manifestations.

The above two criteria for the diagnosis of minor psychoses make such a diagnosis very difficult. The coexistence of organic gastrointestinal disease and neurotic symptoms is well known, and their etiological relationship is often difficult to evaluate. Even with very painstaking investigation, organic disease may not be correctly diagnosed and the cases managed as neuroses. The causes for such errors have been reviewed elsewhere.<sup>14</sup> Even more difficult, however, is the finding of adequate psychogenic causes without which therapy is often futile. The chief reason for this difficulty is that our present psychopathology is definitely unsatisfactory and, when subjected to scientific criteria of proof, is not completely convincing even to the most sympathetic observer with the objective method of thinking. However, there is general agreement that for therapeutic purposes the

diagnosis of psychoneuroses and neuroses implies the absence of any primary structural or chemical disease; the existence, in the majority of cases, of a certain constitutional make-up (the predisposing causes); the occurrence of precipitating or exciting causes; and the formation of symptoms which may be in the psychic or in the physiological sphere, or in both. The constitutional factors may be inherited or acquired. In the "neurotic personality" the neurosis is "built into the character" and is characterized by manifestations intermediate between normal character traits and neurotic symptoms (Jones<sup>19</sup>). Symptom formation results from the action of some exciting cause which may be an injury, infection, a chemical disturbance, or some emotional stress. The symptoms may continue long after the exciting cause ceases to operate, and thus represent release phenomena of the neurotic traits of the previously apparently well integrated personality. These symptoms include either frank anxiety states or symptoms tending to avoid anxiety such as conversion, compulsive-obsessive neurasthenic reactions.<sup>20</sup> These symptoms vary in severity from a slight headache, increased fatigability and irritability, to devastating visceral disturbances, intractable insomnia with marked agitation, and alarming loss of weight. The clinical manifestations frequently overshadow completely the primary constitutional factors or the immediate precipitating mechanisms.

*Anxiety* is the central symptom of nearly all the neuroses and psychoneuroses and is of fundamental importance in the management of all neuroses. Anxiety may be defined as one of the clinically important major emotions recognized introspectively as an unpleasant feeling, accompanied by fear without any, or without adequate cause; and manifested objectively by normal changes in the neuromuscular, autonomic, and secretory functions (emotional expressions). All neurotic symptoms are derived from anxiety arising in the conscious or unconscious parts of the personality. These symptoms include frank anxiety or conversions and substitutions for anxiety reflected in disturbances in the physiological or emotional spheres.

There are many *mechanisms* by which anxiety is converted into symptoms and those interested will search for these in publications on psychopathology.<sup>9</sup> Here it is worth stressing the rôle that *hostility* plays in a good many neurotic conditions. Anxiety gives rise to hostility, which in turn generates more anxiety and thus a vicious circle is established. Both the anxiety and hostility are experiences of which the patient is not at all or only poorly aware. The existence of both anxiety and hostility helps to explain the reasons why "the neurotic person may at the same time be driven imperatively toward dominating everyone, toward complying with others and imposing his will on them, toward detachment from people and craving for their affection. It is these utterly insoluble conflicts which are most often the dynamic center of the neuroses. The two attempts which most frequently clash are the striving for affection and the striving for power" (Horney<sup>21</sup>).

It is necessary to emphasize two other factors:

(a) *A given group of symptoms (such as gastrointestinal or cardiac) is only a conspicuous part of the total neurosis.* The symptoms can rarely be successfully treated without evaluating the total situation.

Just what determines the occurrence of disturbed function in some organs and not in others is not definitely known. The choice of the organ involved may be traceable to one or more of the following factors:

(1) An inherited structural or functional inferiority of some organ (Adler<sup>22</sup>).

(2) Acquired constitutional traits through early inhibitions and frustrations, especially in the psychosexual spheres, possibly the formation of complicated conditioned reflexes; and

(3) Incidental but frequently precipitating causes which often act through auto- and hetero-suggestion and other psychic mechanisms in a manner entirely unknown to the patient, but having a definite relation to some experience or phantasy in earlier life.

(b) The various symptoms and their special etiology, psychopathology, prognosis and treatment differ somewhat in the several types of neuroses.<sup>23</sup> These types include anxiety neurosis, conversion hysteria, anxiety hysteria, neurasthenia and compulsive-obsessive reactions. The description of these various types, as well as the borderline conditions such as gastric ulcer and ulcerative colitis will be more conveniently discussed under the heading of treatment. Here it may be stated and emphasized that the various functional gastrointestinal disturbances may occur in any of the five types mentioned, and that their etiologic, psychopathologic and therapeutic factors differ widely. Psychotherapy concerns itself not so much with "the symptoms" anorexia, esophagospasm, cardiospasm, pylorospasm, bulimia, painful affections, pyrosis, globus hystericus, mucous colitis, irritable bowel, vomiting, diarrhea, constipation, hiccups, aerophagia, etc., as with the *emotional reaction* responsible for the physiological disorders or abnormal personality attitudes.

*The Attitude of the Physician to the Problem of Diagnosis and Treatment.* The management of the neuroses imposes upon the modern scientifically minded physician many hardships and even punishments. He was nurtured, and assumes himself living in an atmosphere of precision with controls in diagnosis and treatment. This scientific atmosphere does not yet exist in the psychopathology or treatment of the neuroses. In the management of the neuroses he must use an entirely different technic. If he is, and he should be, of a critical type of mind, he finds great difficulty in dissociating himself from his "organic" leanings despite all his efforts to the contrary. But even if he is willing to accept the teachings of psychopathology and has a working knowledge of this subject, he is confronted

with the most difficult aspect of the problem, namely the *time element necessary for examination and treatment*. The management of most of the common neuroses requires much time, which those practicing medicine cannot spare. Lastly, it is necessary to emphasize that some physicians are constitutionally unfit to manage neuroses, just as some physicians cannot be good surgeons, obstetricians, or pediatricians.

*Some Principles in Treatment.* There are many schools of thought concerning the treatment of the neuroses. There are still those who attribute the neuroses to *organic* conditions and accordingly stress the importance of the removal of foci of infection, prolonged physical rest, tonic medication, physical therapy, and change of environment. Some hold that persuasion and rationalization will cure most neuroses. Others depend on suggestion (including hypnosis), and still others on the so-called individual psychology, analytical psychology, group analysis and Freudian analysis or some of its several modifications. Some of the systems of treatment are totally unsuitable except for those who devote their time exclusively to psychotherapy. Most neuropsychiatrists use one system with their individual modifications.

The suggestions for treatment here presented may be utilized by those not specializing in neuropsychiatry. Such treatment will take care of some of the common neuroses such as anxiety neurosis, conversion hysteria, and some cases of anxiety hysteria. Many cases of anxiety hysteria and nearly all obsessive-compulsive reactions should be treated by qualified neuropsychiatrists.

As in other branches of medicine it is better to know and employ a *few procedures well* rather than to resort to many procedures in a haphazard fashion. Possibly in no branch of medicine is treatment less understood or systematized. Haphazard treatment not only decreases the benefit to the patient but does not improve the physician's acumen. On the other hand, if the physician becomes skilled in the employment of a few procedures he will eventually acquire new ones and will finally become a good therapist.

For purposes of treatment we may compare a neurosis with some acute infectious process, such as pneumonia. In the latter disease the fundamental process is the systemic infection with pathological lesions predominantly in the lungs and accompanied by annoying symptoms such as pain, cough, and an unpleasant systemic reaction. In the neuroses a similar state exists. The primary process, however, is in the realm of emotions and only mild secondary physical disturbances accompany the state. The basic principle in the treatment of pneumonia is to overcome the underlying infection, and at the same time, the annoying symptoms are allayed by various means. In the treatment of the neuroses exactly the same principles are followed. To the psychotherapist the emotional disturbances, conscious or otherwise, have just as much significance as does the infection to the physician treating the pneumonia. The therapist must have this approach if he is to be successful with his patients. If the therapist has



such an attitude he is not likely to state to the patient at the conclusion of the physical and laboratory investigations: "There is nothing the matter with you. I can find nothing wrong with you. Don't be crazy; forget about it and snap out of it." He should rather say to himself: "It is now my business to determine the emotional factors which produced the soil, and facts in the evolution of the tension and disguises reflected by the patient's complaints."

The treatment varies with the several types of neuroses. The discussion will be considered under the following headings:

- A. Psychotherapy applicable to most common neuroses.
- B. Treatment of symptoms.
- C. Treatment of anxiety neurosis.
- D. Treatment of conversion hysteria.
- E. Treatment of anxiety hysteria.
- F. Treatment of compulsive-obsessive reaction.
- G. Treatment of borderline conditions—peptic ulcer and ulcerative colitis.
- H. Treatment of organic gastrointestinal disease, complicated by neurosis.

*A. Psychotherapy.* This is useful in the treatment of all neuroses and neurotic manifestations complicating physical disease, but is especially useful in anxiety hysteria (sometimes called neurasthenia, anxiety state or nervous exhaustion).

Psychotherapy is a procedure which aims to correct the underlying psychopathological difficulties, as well as the various symptoms of which the patient complains. It is a psychological device used to change the attitude of the patient toward himself, toward his physical and mental processes, and toward his environment. It is an attempt to reevaluate his various life problems in relation to his various symptoms in the light of intellectual but, especially, emotional experiences. For descriptive purposes psychotherapy is divisible into several artificial stages.

1. *Rapport.* This is a relationship between physician and patient whereby the latter gains confidence in and respect for the therapist, and at least a desire to coöperate despite preconceived notions of the origin of his symptoms. Rapport is indispensable for successful treatment and is probably the most important step in the treatment. To attain the attitude of a satisfactory rapport the patient must feel that the physician not only sympathizes with him, but also that he has a clear formulation of his case and has the ability to help him. To justify to the patient's expectations the physician must not be too hasty in arriving at conclusions but once the formulation is made he must remain firm in his statements, betray no doubts or indecisions, and above all be frank and truthful.



The establishment of rapport begins with the taking of the history. The history should be complete and should be recorded at once. The patient should be given ample time to tell his story even if repeated visits are necessary. The physical examination should be complete. Necessary laboratory procedures should be made, and at times some special examinations such as roentgen-ray of the skull, electrocardiograms or gastrointestinal roentgen-rays should be made even though in the clinician's judgment such examinations are not necessary. Once the physical investigations are completed and found negative, *reëxaminations are most inadvisable* since they unsettle the patient.

At this point the physician is in a position to inform the patient that his symptoms are not due to physical causes but emphasize that his complaints are undoubtedly due to other factors which are in need of treatment. Without being specific the average patient will understand the statement that just as physical causes result in emotional disturbances so emotional disturbances may cause physical derangements, and that irrespective of origin, the patient's disability requires medical treatment. One may add that the human mind is at least as complicated and intricate as the human body and that disturbances of either are problems for treatment. Some common sense examples of effects of fear and the other major emotions may be given at this point. It may also be necessary to state that absence of physical causes does not mean that the patient is insane or that he "imagines" his symptoms. Above all at this point the patient must be assured that he will get well although progress be imperceptible at first and that he will have to help the physician actively in the treatment.

The patient is next given the general statement that his individual symptoms are undoubtedly a source of unhappiness and will receive palliative treatment just as cough and pain in pneumonia would be treated. He should be made to understand that the success of the treatment depends upon tracing and correcting unusual attitudes and reactions of his personality of which the presenting symptoms and nervous tension are conspicuous manifestations.

2. *Ventilation or aeration.* This consists in bringing into conscious attention in specific detail unwholesome attitudes and reactions which are usually associated with irritating memories. Some material is usually elicited in a detailed initial history. More information will be given by the patient when he is permitted to talk freely in direct interviews. Often, however, it is necessary to use the free association method. It should be stressed that ventilation is not merely a diagnostic procedure. Its goal is to give the patient the opportunity to discharge and bring out in the open all possible life experiences and phantasies which might have been causing him difficulties either consciously or unconsciously.

Ventilation should be supplemented by procuring from outside sources all possible information regarding the experiences and reactions of the patient, and the actual environmental factors in which he lives.

3. *Desensitization.* This consists in removing by intellectual discussion the unpleasant emotional tone attached to the irritating memories. The patient is encouraged to face openly the unpleasant experiences and memories of the past. To accomplish this the material must be brought into consciousness repeatedly. This is done either by direct interview or by the free association method. In the course of time there is usually a better objective understanding by the patient and, what is more important, the emotion loses its unpleasant "sting."

The physician should guide the patient in this phase of the treatment. An element of suggestion is neither avoidable nor undesirable provided the therapist does not abuse it. It is necessary that the desensitization should be gradual to avoid severe "shock" reaction, and prevent undue wounding of sensitivity and pride and slowly build up tolerance to unpleasant emotional realizations.

It is best to leave most patients with some formulation at the end of each treatment period.

4. *Retraining, reëducation and stabilization.* This consists in guiding the patient to react more or less *automatically* in a symptomless, efficient and wholesome manner to various stresses in life. The responses to be more or less automatic must be free from unpleasant emotional tone which is accomplished by desensitization and must be learned, at least in the adult, by persistent conscious effort. As a necessary part of lasting successful retraining and reëducation the patient should be guided in formulating an economic, social and recreational plan which will vary markedly with the individual patient.

5. *Psychotherapy of family.* It is often necessary to desensitize the various members of the family to the patient's illness and reëducate them into new modes of response toward each other and toward the patient.

6. *Compromise formation.* The neurotic situation is often complicated by various stresses such as marital, economic or social problems which cannot be eliminated. The patient should be made to face the facts of the situation and work out some compromise for himself.

*B. Treatment of Symptoms.* In addition to gastrointestinal the more common and important symptoms of neuroses consist of general tension and anxiety, abnormal fatigability, insomnia, fears of death and insanity, complaints referable to the heart, and pains in various parts of the body. Theoretically symptoms, as such, should be ignored since they are merely manifestations of the underlying psychopathological process at which our main therapeutic attack is directed. Practically, it is often necessary to pay wholesome attention to the complaints.

Certain general principles in the treatment of symptoms should be observed. They are:

(1) *Avoid unnecessary surgery.* Focal infections play no rôle in the fundamental psychopathology of neurosis. For example, the removal of

doubtfully diseased tonsils should not be preceded by the promise that it will cure the neurotic manifestations. The removal of a large fibroid tumor should be preceded by statement that it will probably have no effect on the lasting gastrointestinal or other symptoms such as the fear of insanity, abnormal fatigability, and daily headache which have existed for 10 years.

(2) *Explain to the patient the evolution of the symptoms from faulty emotional reactions.* Do not tell him they are imaginary and that he should forget them. If circumstances permit, some explanation should be given of how anxiety may give rise to such physiological disturbances as tachycardia, vomiting, crampy pain, frequent mucous stools, etc. Tell him that medication, dietetic treatment, etc., are given only for the *secondary* manifestations and will not affect the basic disturbance. For the same reason *avoid ritualistic procedures* (including diet ceremonials) which tend further to complicate the already muddled existence of the patient.

(3) *Physiologic and psychologic symptoms should not be neglected* while the patient is under psychotherapy. It is true that as ventilation and desensitization reach a satisfactory level the symptoms will become less severe, but it is equally true that:

(a) A markedly tense, anxious and restless patient will be benefited by removal from home to a hospital or sanatorium.

(b) General weakness and easy fatigability will be allayed by rest in bed from a day or two to two to four weeks. The fatigue should not be ascribed to actual overwork which by itself is rarely a cause of neurosis.

(c) Malnutrition requires proper alimentation, vitamins, tonics, etc. Gastrointestinal symptoms, though secondary, should be corrected by a suitable dietary regimen until the patient "finds himself." The use of alcohol, tobacco, and coffee should be considered.

(d) Insomnia should be treated with great care. *The psychoneurotic, unlike the manic-depressive individual, is apt to become a drug addict.* Nevertheless, in the early acute stages of a neurosis or of a recurrence of a neurosis, somnifacients at night and sedatives through the day are almost indispensable. As the tension disappears it will be easy in the majority of cases to eliminate the use of somnifacients and sedatives.

(e) Phobic and panicky attacks are best not treated by medication as this often interferes with psychotherapy. In some cases phobic symptoms actually can be cured by deconditioning and training, and at least one should not encourage fear reactions by giving them false crutches.

Before proceeding with discussion of the several types of psychoneuroses it is wise to indicate that from a psychopathological standpoint the underlying process may vary in *depth* and *extensity*. Thus, the state characterized by functional manifestations having their origin in situations in the immediate present or recent past and occurring in an otherwise well integrated individual is called a *neurosis*. When the *predisposing* causes are due to deep-seated personality difficulties the resultant condition is a psychoneurosis,

even though the exciting cause may be quite superficial. It is obvious that the more extensive the psychopathological distortion the more difficult will be the treatment. As in other branches of medicine, types are not always pure and mixtures are common.

*C. Treatment of Anxiety Neurosis.* By anxiety neurosis is meant an episodic occurrence of anxiety, accompanied by somatic symptoms, especially palpitation, trembling, sweating and general weakness, less frequently by vomiting and diarrhea, and by complete or nearly complete freedom from symptoms between attacks. The precipitating causes of anxiety neurosis are in the immediate present or in the recent past. The most common causes are unsatisfactory sexual experiences (such as coitus interruptus, sudden cessation of masturbation in late adolescence, etc.) or threats to economic or social security.

The vomiting of children in the early grades which occurs only on school days belongs to this type of reaction. Similarly diarrhea of students at examination periods, and the vomiting of those who fear illegitimate pregnancy, reflect the abnormalities of an anxiety neurosis.

The *treatment of anxiety neurosis* is usually satisfactory. The cause should be removed if this is at all possible. When the cause cannot be removed, the patient must develop substitutive activities such as new interests and recreational outlets, and in some cases compromise formations.

*D. Treatment of Conversion Hysteria.* Conversion hysteria is characterized by the presence of motor, sensory, visceral, and episodic phenomena (conversion symptoms) accompanied by little or no anxiety, not due to any primary physical or biochemical abnormality and traceable to some definite psychogenic cause.

Conversion hysteria occurs in individuals who are hypersuggestible and emotionally immature. In conversion hysteria there is always a *motive* either to obtain something otherwise unobtainable or to escape a situation which is unbearable. The ordinary traumatic neurosis has a large element of conversion hysteria, the motive for which is not difficult to find.

Other precipitating causes in this group of cases are usually not difficult to find, and are often related chiefly to marital difficulties, death in the family, to a feeling of economic or social insecurity, or to many other life situations.

The most common gastrointestinal symptoms encountered in conversion hysteria include globus hystericus, vomiting, aerophagia, hiccups and diarrhea but nearly any other physiological disturbance may be present.

*Suggestion* in some form is probably the first method of treatment to be employed in these cases. Attempts at compromise formation in marital and economic difficulties also require and deserve considerable attention. The end result in these cases is usually good provided the cause can be removed or the patient be induced to make some compromise.

*E. Treatment of Anxiety Hysteria* (neurasthenia, anxiety state, nervous exhaustion). Anxiety hysteria is characterized by a variety of somatic



complaints not due to primary physical or biochemical causes, accompanied by diffuse anxiety or by phobic phenomena, and traceable to psychogenic, often unconscious, causes.

Constituting over 60 per cent of all cases, anxiety hysteria is the commonest of the psychoneuroses and neuroses. It is variously designated as neurasthenia, anxiety state, or nervous exhaustion. Anxiety hysteria occurs in the oversensitive and hypochondriac type of neurotics. It is the most common psychoneurosis encountered in gastrointestinal practice and constitutes a considerable percentage of this practice. It is in anxiety hysteria that one encounters esophagospasm, cardiospasm, pylorospasm, mucous colitis, pyrosis, aerophagia, alternating constipation and diarrhea, and a variety of painful reactions. Apprehension is a constant companion of these symptoms.

The predisposing causes are deep seated in the personality, frequently related to the early psychosexual life, whereas the precipitating causes are related to the numerous life situations.

The treatment of anxiety hysteria is often difficult. Some cases can be treated by the methods outlined in this presentation but not a few require intense psychotherapy in the form of analysis.

*F. Treatment of Compulsive-Obsessive Reactions* (psychasthenia). Compulsive-obsessive reactions are characterized by the existence of irrepressible thoughts and irresistible impulses designed to avoid anxiety, by the patient's recognition of the absurdity of these thoughts and impulses and by the appearance of anxiety when the patient attempts to "disobey" the thoughts and impulses. The personality history shows a very definite neuropathic trend. This becomes more evident when even a partial analysis is attempted. By this method neurotic traits are found to have existed since childhood, but were thoroughly integrated in the personality make-up and did not produce disability symptoms until somewhat later in life. The precipitating causes can only be ascertained by a partial analysis and then are to be found largely in the psychosexual sphere. It is in this form of psychoneurosis that any treatment short of partial analysis is of little value.

Gastrointestinal disturbances are rare in the compulsive-obsessive reactions.

*G. Treatment of Borderline Conditions, Peptic Ulcer and Ulcerative Colitis.* The rôle of emotional factors in peptic ulcer and ulcerative colitis remains a moot question. There can be no doubt that emotional disturbances *aggravate* existing lesions and there is good reason to believe that emotional strain may reactivate quiescent lesions.

It would seem that peptic ulcers occur in individuals whose makeup may be characterized by rigidity, over-conscientiousness, and even intolerance, in individuals who are overly honest and meticulous, usually dynamic and often aggressive but who do not develop compulsive-obsessive tendencies. One may suggest that the prolonged nervous tension and anxiety could result in disturbances of secretion and motility leading to peptic ulcer, but proof is



lacking that such is the mechanism. However, there is some evidence that cerebral lesions, principally in the diencephalon, are associated in the ulcerations in the gastrointestinal tract.<sup>24</sup>

Based on personal observation of a few cases and on a study of the literature, I am unable to formulate a type of personality or definite psychological mechanisms that could be considered as primary causes of *ulcerative colitis*.

*H. Treatment of Organic Gastrointestinal Disorders Complicated by Neuroses.* The problem of neurotic manifestations complicating organic gastrointestinal diseases is not vastly different from similar complications in other organic diseases. Such neurotic manifestations may *antedate* the organic disorders and indeed may act as precipitating or aggravating factors in such diseases as peptic ulcer or ulcerative colitis. On the other hand, the organic disorders may bring out *latent* neurotic traits which may interfere with recovery and convalescence and indeed may last long after the organic lesion has been arrested or eradicated. The neurotic manifestations may be quite frank or may be masked. In the latter event the suspicion of the complicating neurosis is aroused when the patient's attitude does not correspond to evidences of improvement of the physical disease.

It is in these cases of organic disease complicated by neurotic complications that the psychotherapist must exercise utmost caution, acumen, and judgment. In the first place he must be enough of a clinician to evaluate the *organic phases* in relation to the total situation. He must next be able to evaluate the *personality pattern* harboring both the organic and neurotic factors. He must then bring out and evaluate the *psychogenic factors* which may be responsible for the neurotic manifestations. The consideration of the psychogenic factors is complicated by the following situations:

(a) In not a few organic cases *superficial inquiry* fails to disclose any emotional difficulties. Indeed, single or brief interviews may lead to the erroneous conclusion that the individual has no emotional problems. This may be due to the patient's own ignorance of his situation or to his unwillingness in the presence of organic disease to establish a rapport with the psychotherapist necessary for psychological investigation. The psychotherapist himself may be influenced by the organic factors to such an extent that his usual persistence may be discouraged.

(b) The discovery of psychogenic factors of remote or recent past, or even immediate present, need not lead to the *conclusion that such factors are responsible* for the neurotic manifestations. Such fallacious reasoning is harmful enough in the management of the uncomplicated psychoneuroses but is therapeutically disastrous when practiced in cases with organic disease and leads to considerable resistance and actual unhappiness on the part of the patient. It is not the many and varied unpleasant incidents and situations which occur in many individuals' lives which determine the formation of

neurotic symptoms but "the patient's ability to adjust to such situations, especially his reactions to them, the degree of pent-up anxiety, the nature and seriousness of his conflicts, that must be evaluated."<sup>25</sup>

(c) After a careful evaluation of significant psychogenic factors, desensitization and new adjustments should be made gradually and with much caution. The neurotic with organic disease is even less willing to abandon his personality tendencies than is the uncomplicated neurotic. It is in these cases that "compromise formations" are most needed and difficult to achieve. It is as often as much a problem for the internist as for the psychiatrist and indeed the psychiatrically minded and *trained* internist can often do it better than the average psychiatrist.

#### SUMMARY

The so-called functional disorders of the gastrointestinal tract are disturbances in motility, secretion and sensation of this tract caused by dysfunction of the vegetative nervous system in its various ramifications. Such disorders may be due to a number of causes among which psychological factors are common and important. The diencephalon probably plays a major rôle in the conversion of psychic disturbance into gastrointestinal manifestations by reason of its being a center for several related functions.

In the psychotic reactions, gastrointestinal symptoms are common. Early, especially in schizophrenia and involution melancholia, the gastrointestinal manifestations may mask the fundamental disease process. Mild psychotic reactions, especially depressions, may go unrecognized by reason of the preponderance of the gastrointestinal symptoms. The treatment should be directed to the underlying psychotic condition.

In the psychoneuroses and neuroses the gastrointestinal manifestations may be the conspicuous manifestations of the total neurosis. To treat these cases the physician must have a minimal knowledge of psychopathology with some formulations regarding the structure of personality, various types of reactions, the nature of anxiety and its various modifications, and learn to understand his patient in terms of symbolizations and tensions. He must be prepared to devote considerable time to enable him to have a clear formulation of the problems of the individual patient.

The success of treatment, in the majority of cases, depends upon some evaluation of the underlying psychopathology and a thorough knowledge of a few therapeutic procedures applicable to most psychoneuroses and neuroses and special procedures in the treatment of some types of neuroses and symptoms.

The several types of neuroses and psychoneuroses vary in their symptomatology, etiology, psychopathology and treatment.

What not to do in the treatment of the psychoneuroses and neuroses is also important.

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## FEVER THERAPY \*

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WITHIN recent years more than 600 articles have been written on artificial hyperpyrexia and more than 50 diseases have been allegedly treated by this method of therapy. It is not my intention to condemn any fever producing method used, to criticize any member of the profession for using any particular type of fever therapy which he may prefer and can best use, or to offer artificial fever therapy as a panacea for the correct and proper treatment for all diseases. I do intend briefly to review the current literature on the subject, to describe the method of treatment I have been taught to use in the Navy, namely, artificial fever therapy produced by the Kettering hypertherm cabinet, and to report the results I personally have obtained in a series of cases of neurosyphilis and gonococcus infections during this year.

At the present time the most widely recognized therapeutic fever producing agents are:

1. *Foreign Proteins, viz., Typhoid and Paratyphoid Vaccines, Given Intravenously.* However, these will not produce and maintain the necessary elevation of temperature desired, and consequently their use in the treatment of neurosyphilis, gonorrhea, and other diseases in which a high elevation of temperature is desired is of little practical value and has largely been replaced by the safer and more accurately controlled artificial fever by physical means.

2. *Malaria.* Malaria was tried in Russia in 1937 for the treatment of gonorrhea; the patients' symptoms did not improve but were exaggerated. This treatment will not maintain a rectal temperature of 106° F. over a period of several hours and would, therefore, be of little value in the treatment of gonorrhea. On the other hand, malaria has been recognized for many years to be of definite proved value in the treatment of certain stages of syphilis, particularly dementia paralytica. Such authorities as John A. Kolmer, George Wilson and Paul O'Leary still prefer malaria to the artificial physical methods of producing hyperpyrexia.

Two factors which may interfere with the immediate use of malaria are its unavailability in certain localities and the patient's physical condition. Another factor to consider at this time is the increasing shortage of quinine, as this drug may be required to control the therapy of induced malaria.

From the clinical data available it appears that there is very little difference in the results obtained from the use of malaria and the use of the hypertherm cabinet in the treatment of dementia paralytica. However, it is interesting to note that Ewalt and Ebaugh<sup>1</sup> in reporting 232 cases of de-

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mentia paralytica treated by both methods of therapy state that the artificial fever series was safer and produced the better results; also when contraindications to malaria were present, many cases could be safely treated with artificial fever therapy. Huntley<sup>2</sup> of Michigan in a series of 168 men with dementia paralytica who completed treatment, reports that he obtained 100 per cent clinical improvement and 83 per cent of serological remissions with artificial fever therapy. This work was done in a state prison where he had complete supervision of his patients with follow-up chemotherapy. With 29,726 hours of fever treatment he does not report a single fatal accident attributable to fever therapy. Neymann<sup>3</sup> reports that two-thirds of a total of 114 cases of tabes dorsalis exhibited definite improvement after fever therapy. Krusen<sup>4</sup> asserts that one of the most constant findings when physical fever is used in treatment for tabes dorsalis is the relief of gastric crises and tabetic pains. He also states that the best results are obtained in early cases, both with tabes dorsalis and dementia paralytica. Interstitial keratitis, non-specific iritis and uveitis are said to respond readily to fever therapy.

My personal experience with the treatment of neurosyphilis has been limited. Available studies show that about 70 per cent of cases of dementia paralytica when properly treated with either malaria or physical means show marked improvement. It seems advisable to use the method of treatment and equipment which are most convenient and with which one is most familiar. Both malaria and artificial fever therapy are dangerous and should only be used in an institution with properly trained personnel and standard equipment.

3. *Artificial Fever Therapy by Means of the Kettering Hypertherm Cabinet.* A few months ago Turville and Fetter<sup>5</sup> reported 1101 fever treatments given to 173 patients in the Naval Hospital in Philadelphia during the two-year period July 1, 1940, to July 1, 1942. Of 38 patients treated for gonococcic infections they reported 87 per cent cured. Marked improvement occurred in 71 per cent of 32 patients treated for neurosyphilis. On the basis of their studies they believe that fever therapy is the treatment of choice in sulfanilamide-resistant gonococcic infections and in dementia paralytica, and is a valuable adjunctive treatment in other diseases. They further believe that the blood chlorides and nonprotein nitrogen are not disturbed to a point of danger if the patient takes and retains the prescribed amount of water and sodium chloride before and during the fever session.

Kendell, Rose and Simpson<sup>6</sup> have reported marvelous results in a series of 31 unselected consecutive chemotherapy-resistant gonococcic infections treated by the combined method of artificial fever and chemotherapy. They reported 100 per cent cures in this series and stated they used rigid bacteriologic criteria for the basis of determination of this cure. They further reported that the time-dosage relationship greatly influenced the effectiveness of this method of therapy. When the drug is administered for 18 hours preceding fever treatment, the effectiveness is much greater than when it is



administered immediately prior to or during treatment. The blood concentration of the drug in the patient should be 1:10,000 or roughly 10 mg. of the drug per 100 c.c. of blood at the time of the fever treatment. As shown by Wengatz, Boak and Carpenter,<sup>7</sup> the thermal death time of certain strains of gonococci is lowered by approximately 50 per cent in the presence of a concentration of 1:10,000 sulfanilamide. On this assumption Simpson and his co-workers tried this therapy and reported their findings. These 31 cases were given a single 10-hour session after they had been on sulfanilamide for 18 hours and the blood concentration levels were approximately 1:10,000.

I have two series of my own cases to report. The first series consists of 23 cases of gonococcal infection treated at the National Naval Medical Center in Bethesda, Md., in the early part of this year. Nineteen of these cases were uncomplicated gonorrhea which were chemotherapy-resistant. All of these cases except two were cured with one long nine-hour fever session with rectal temperature between 106° and 106.8° F. for seven hours. The other two cases required another short session of five hours each given on the third day, after which they were both clinically and bacteriologically cured. Two cases of this series had severe unilateral gonorrheal ophthalmia which responded readily to fever therapy. I have seen four severe cases of gonorrheal ophthalmia which were treated with artificial fever therapy and which responded as well as any disease responds to any type of therapy. One case had a severe panophthalmitis and a good ophthalmologist had recommended evisceration. The patient was given 10 hours of fever therapy at a rectal temperature of 106° F. after proper preparation, and he returned to duty with 20/20 vision in the affected eye. The other two cases in this series had severe gonorrheal arthritis, received 10 five-hour sessions and improved to the extent that they both returned to a regular duty status. All of these cases received combined chemotherapy and artificial fever therapy, the technic of which will be described later. My second series of cases was treated at this hospital since July 1 of this year. It consists of 28 cases of chemotherapy-resistant gonococcal infections and four cases of neurosyphilis. All four of the neurosyphilis cases have shown marked clinical improvement. Further serological studies will have to be made. Twenty-four of the 28 cases of gonococcal infection were cured. In two cases the treatments had to be discontinued. The other two cases have shown very little or no response to this type of therapy.

In addition to the excellent therapeutic effects shown in gonococcal infection and syphilis, Prickman<sup>8</sup> states: "One cannot but be impressed in treating febrile cases of brucellosis by artificial fever, by the promptness of the resulting remissions, the absence of relapses, the almost immediate feeling of well-being, the gain in weight and strength and the patient's ability to return promptly to work. This has occurred in four out of five patients so treated."

## TECHNIC OF FEVER THERAPY TREATMENT USED

This technic of treatment is not original. It is practically the same technic described by Krusen<sup>9</sup> and by Simpson<sup>6</sup> and their co-workers.

The patient is given a complete general physical examination the afternoon before treatment. He should have 24 hours' rest prior to treatment with a high carbohydrate diet and a moderate amount of forced fluids. Urine should be checked for amount and specific gravity for 24 hours prior to treatment.

Eighteen hours prior to time of starting treatment (if the patient is being treated for gonorrhea), he should be given as an initial dose, 4 grams



FIG. 1. Patient with nurse and equipment during the high temperature period of fever therapy treatment.

(60 grains)—or 5 grams if he weighs more than 150 pounds—of sulfathiazole by mouth, followed every four hours day and night with 1 gram. This should bring the patient's blood level to a concentration of 1:10,000 by the time he acquires a high temperature. The patient is not given breakfast, but may have black coffee. A soap suds enema is given for convenience before he is put in the cabinet. It is well to give 1000 c.c. of 5 per cent glucose in normal saline prior to the patient's entrance into the cabinet. The patient should be shown how to use a B.L.B. mask and told he is going to be given oxygen prior to entering the cabinet, so he will know what to expect during the excitable stage. Fluids are not permitted copiously the first hour of treatment because this would precipitate vomiting. After the first hour

the patient is encouraged to drink .5 per cent salt solution, fruit juices and water. These fluids should be chilled but not iced. Pantopon gr. 1/6 to 1/3 and codeine by mouth are the best drugs to use to control pain and restlessness while in the cabinet. I do not use morphine; if it is used it should be in small doses and repeated, never in large doses, during high elevation of

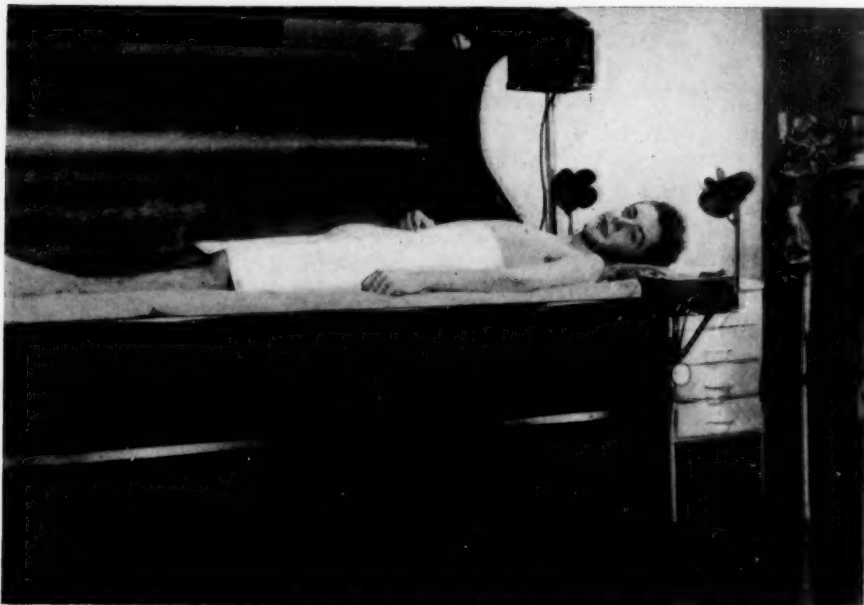


FIG. 2. Patient after receiving 10 hours fever therapy by the Kettering hypertherm method.

temperature. The patient should be watched very cautiously. He should be removed from the cabinet for any of the following reasons:

1. If he becomes unconscious at any time.
2. If the blood pressure drops suddenly and there are symptoms of approaching cardiovascular collapse.
3. If the pulse rate is above 160.
4. If any untoward signs or symptoms you cannot explain develop. Remember the rhyme—"If in doubt, take him out."

*Complications.* (1) Tetany. This is frequent but without bad results. It responds quickly to calcium gluconate. (2) Circulatory collapse. This picture is the same as severe surgical shock. I have seen two cases. The treatment is 100 c.c. of 50 per cent glucose, and supportive treatment. (3) Cramps of various muscles of the body. This can be prevented if patient takes and retains sodium chloride in proper amount. (4) Pulmonary edema. Rare. Treatment is venesection. Remove 500 c.c. of blood. (5) Cerebral edema. Rare. Treatment is spinal puncture.

*Contraindications.* These are the same as for any major surgery.

### CONCLUSIONS

1. Fever therapy in combination with chemotherapy offers the best therapeutic weapon we have in treating gonococcic infections and neurosyphilis, particularly dementia paralytica. It is a valuable adjunctive therapeutic agent in the treatment of chorea, infectious arthritis and brucellosis.

2. After one unsuccessful trial of chemotherapy in all gonococcic infections, I strongly recommend and urge that the combined method of chemotherapy and artificial fever therapy be instituted.

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## THE RELATION OF THE CARRIER TO EPIDEMIC MENINGITIS \*

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By way of orientation, it may be well to review briefly the facts, so far as they appear to be known, regarding the elements involved in the spread of epidemic meningococcal infection. We shall then be in a position to examine the evidence which supports certain of these matters and to call attention to the lacunae which still exist and which make it difficult to outline any reasonable program for control of this disease.

It has long been recognized that the meningococcus finds its normal habitat, as far as is known, in the human nasopharynx. Occasionally, and presumably from this focus, it enters the body and produces a septicemia and a meningitis. Also, and certainly more frequently, it leaves the throat on droplets of saliva expelled in talking, coughing or sneezing and finds a new abode in the nasopharynx of another individual. Careful examination of any large group invariably leads to the detection of carriers. Therefore, conditions favorable to the transmission of other respiratory disease should result in a rise in carrier rate.

During the last war much emphasis was placed on carrier studies. Overcrowding in barracks was shown to result in a gradual rise in the percentage of such individuals, and it was stated by Glover that when a certain critical level was reached, cases of meningitis began to appear. Doubt was later thrown on this by studies carried out by Dudley and Brennan in an English naval training station. During 1932 a number of sporadic cases of meningitis were accompanied by a carrier rate among contacts of only 13 per cent, whereas the following year, with no disease, a rate of 50 per cent was maintained.

Like many other bacterial species, the meningococci are serologically heterogeneous. Their classification is difficult, and even now relatively unsatisfactory. It is generally accepted, however, that Type I organisms are responsible for most epidemic disease, whereas other types are more likely to be encountered in the occasional sporadic case. Carriers of Type I organisms normally make up only a small proportion of the total. Therefore, in order to provide valid evidence, not only must the type of organism causing clinical disease be known, but the carrier strains must also be typed, for only the proportion of homologous organisms can be significant. Failure to provide this information goes far to invalidate a good deal of the older data.

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There is a conviction, not yet entirely supported by experiment, that carriers of Type I organisms tend to be transient, whereas the other types, ordinarily of little or no pathogenic importance, may persist for long periods in their hosts. It is highly probable that many of the carriers who were placed in quarantine, often for months, during the last war, harbored Type II and were quite harmless.

Of Type I meningococci there are probably strains of varying degrees of virulence, and in man there are surely different levels of resistance to infection. Thus, an individual who acquires an organism of this type in his nasopharynx may suffer no ill effect, or he may develop the usual clinical infection of the meninges, or he may succumb within a few hours to a fulminating septicemia. Methods for the evaluation of virulence of meningococci as well as for testing host resistance are urgently needed in order to provide a sound basis for control measures. None of the attempts to reach an understanding of these factors has proved satisfactory, and it is to be hoped that the renewed interest shown at present in the matter will yield information which is badly wanted. Thomas, Smith and Dingle, at the Boston City Hospital and in our own Department have already uncovered certain possibilities which should be capable of application to these vexing problems.

It seems probable that a large proportion of our population is relatively immune to the meningococcus, possibly through harboring organisms of low virulence from time to time. It is also possible that the normal tissues of the nasopharynx provide a barrier which even a meningococcus of high virulence is unable to pass, but which may occasionally break down owing to mechanical injury or to other respiratory infection. In any case, enough information is at hand to offer a satisfactory explanation of certain of the phenomena of an epidemic. For example, it is usually difficult to trace direct contact between clinical cases, and we may assume that this is due to the fact that only an occasional individual who harbors the organism becomes actually diseased. The same virulent strain may, therefore, be passed from one healthy carrier to another through many hosts before it reaches one in which conditions for invasion are suitable. When this does occur, all trace of the intervening chain of passages has been lost.

Clearly, there are many problems for the bacteriologist and immunologist to solve before he is in a position to lay down plans for the control of epidemics. Our own work, thus far, has concerned itself with the rather elementary but essential matter of simplifying the methods used for the isolation and recognition of the meningococcus, and with the collection of data on carrier rates.

Traditionally, cultivation of this organism must be carried out on an "enriched" medium containing sterile ascitic fluid, serum or blood. The preparation of such a medium under field conditions in military units becomes extremely difficult, a fact which every bacteriologist involved in the matter during the last war well remembers. The British at that time used a

medium in which the ascitic fluid was replaced by an extract of dried peas, presumably because of the high protein content of this seed. When properly made, it was entirely satisfactory, but its preparation was troublesome. We have now found that this medium can be greatly simplified. Its efficacy was due, not to the protein of the pea meal, but to the starch. Ordinary laundry or corn starch is effective, and the complete medium can be readily prepared from ingredients easily obtainable. It can be autoclaved and stored and is well suited to field use.

Another most troublesome matter was the fact that the meningococcus very quickly dies on a swab when chilled. It was customary, therefore, to carry the culture medium in Petri plates to the site at which cultures were to be taken. They were transported in water jacketed cases kept at body temperature, inoculated directly, and kept warm until they could be returned to an incubator. This difficulty, and the accompanying limitation of the number of cultures which could be taken, has now been overcome. Cox, McDermott and the writer have shown recently that *gonococcal* material for culture can be preserved even for two or three days, over a considerable temperature range, by immersing the swab in a few drops of sterile horse blood, thus making possible shipment of specimens through the mail. We have found this equally applicable to the meningococcus, and by this means have materially simplified the matter of carrier examinations in the field.

Typing of the strains which are isolated is carried out by a rapid and simple method which I believe was devised by Julia Parker and Zinsser many years ago, and appears not to have been published. It makes possible the ready identification of Type I, many strains of Group II and the new Type II alpha. We have made no effort to classify the remaining strains, which are probably of no epidemiologic importance, but place them in "Group X."

These methods have been used in our laboratory for more than a year in following the carrier incidence of two fairly large communities. About 100 cultures are taken twice weekly from each of these, and worked through. The following table shows the result of this study.

TABLE I

	% Total	% I
Jan. 1942.....	18.6	3.1
Feb. 1942.....	21.7	2.5
Mar. 1942.....	25.7	3.6
April 1942.....	29.0	4.9
May 1942.....	25.0	3.6
June 1942.....	22.8	3.6
July 1942.....	30.1	5.1
Aug. 1942.....	20.6	3.3
Sept. 1942.....	24.4	3.6
Oct. 1942.....	28.7	2.6
Nov. 1942.....	29.4	3.8
Dec. 1942.....	32.7	7.4
Jan. 1943.....	25.6	10.1

In order to condense the data, only the total carrier rate for all strains of meningococci and the Type I figures are given. Those relatively few

cases of the disease which have occurred in these communities during the period of time covered and from which we have been able to get cultures, have all been due to Type I. It is noteworthy that the total carrier rate has been remarkably constant, showing no evidence of seasonal variation. Equally striking is the low and constant incidence of Type I carriers up until two months ago. The rise since that time is definite and may well prove to be significant.

We have recently had an opportunity to cooperate in a study of the carrier situation in another community of individuals living in relatively close contact, during the course of a rather sharp outbreak of Type I infections. Between 60 and 70 per cent of a group of several hundred who were cultured were found to be carriers of the same type.

The problem of what to recommend, in a situation of this sort, is difficult in the extreme. One must naturally adopt the usual measures for minimizing respiratory transfer. Actual quarantine is probably out of the question. An experiment carried out on a group of approximately 400 of these individuals provided remarkably interesting evidence of one possibility which, however, is not without its drawbacks. Half the members of this group were fed sulfadiazine on three successive days, three grams the first and two grams each on the following days. The other half of the group served as a control. Three days after cessation of the drug all were cultured. The Type I carriers in the control group had increased from 68 per cent to more than 70 per cent. Of the 200 who had received sulfadiazine, not a single one carried a meningococcus of any sort. After a further lapse of three weeks, cultures were obtained on 116 of those treated with sulfadiazine. Of these, 18, or about 16 per cent, were found to be carrying Type I meningococci. Remarkably enough, nine of these 18 occurred in the throats of men who had been negative on the initial culturing. In other words, half of the men who have acquired a Type I meningococcus in the three weeks' interval are from the group of 32 per cent originally negative. This would appear to afford some support for the view that transient contact with this organism leads to a measure of resistance against it.

It appears, therefore, that in an emergency it may be possible to eradicate carriers from a given group of individuals, at least temporarily. One would have to balance the necessity against the possible dangers of such a procedure before undertaking it. Except for such a method, no means is known for artificially clearing up the condition.

Fortunately, the mortality of meningitis has been greatly reduced by the use of the new drugs. In spite of this, it remains a distinctly serious disease, and one must hope for advances in our knowledge of its immunology which can lead to more effective measures for its elimination.

## CARCINOMA OF THE LUNG; A REVIEW OF 31 PROVED CASES AT THE PHILADEL- PHIA NAVAL HOSPITAL \*

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### INCIDENCE AND ETIOLOGY

THE outstanding fact about primary carcinoma of the lung is the amazing increase in its frequency during the past 30 years. Formerly bronchogenic carcinoma was considered one of the rare forms of cancer; now it has been found to be one of the commonest. Some startling facts about the frequency of this disease that were brought out by Overholt and Rumel<sup>1</sup> in a recent review of the subject are: (1) that large autopsy series show that approximately 10 per cent of all cancers start in the lung; (2) that about 15,000 people die from bronchogenic carcinoma each year in the United States; and (3) that the lung is now the second most common site of origin of primary malignancy, being exceeded only by the stomach. In fact, Halpert,<sup>2</sup> on the basis of a 10 year survey of necropsies at the Charity Hospital in New Orleans, predicts that carcinoma of the lung will soon be the commonest malignancy in the male, more frequent even than carcinoma of the stomach.

With such an astounding increase during the past three decades in the number of cases of this disease that are being diagnosed, both ante- and post-mortem, it is natural that causes for this are being looked for. A few pathologists still believe that the increased incidence is apparent rather than real. By this they mean that more cases are being found now because they are being looked for by pathologists and clinicians who are "bronchogenic carcinoma conscious," but that actually there has not been an increase in the number of cases during the past four to five decades. However, the majority opinion among both clinicians and pathologists is that the present high incidence of primary lung cancer represents an actual increase in its frequency.

As to the real cause of the disease, or even reasons for the sudden jump in its incidence, we are still pretty much in the dark. The only etiologic agent that seems to be a definite factor does not apply to the great number of people who develop the disease. This factor is the inhalation of radioactive substances. At the Schneeberg mines, where pitchblend is obtained as a source of radium, 62 per cent of the workers are reported<sup>3</sup> to develop carcinoma of the lung. Factors proposed<sup>3</sup> which are more widely applicable as a cause of the disease, and incidentally of its increased incidence are: the influenza epidemic of 1918 (metaplasia of the bronchial mucosa has been found in patients dying of influenza), inhalation of irritating fumes such as

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exhaust from automobiles or fumes from tarred roads or tobacco smoke (the fact that carcinoma of the lung is at least four times as common in men as in women has been cited in support of the tobacco smoke theory), silicosis, tuberculosis, and other non-specific lung infections as bronchiectasis or lung abscess. However, no one has been able to establish any of these agents as being really important as a cause of the disease, or as a cause of its increased incidence. As is the case with most cancers elsewhere in the body, we are still basically ignorant of the cause of primary carcinoma of the lung.

#### CASES SEEN AT THE PHILADELPHIA NAVAL HOSPITAL

In the 21 month period between January 1, 1941, and October 1, 1942, there have been 31 proved cases of primary carcinoma of the lung admitted to the Naval Hospital in Philadelphia, and 16 more cases in which this diagnosis was established to the satisfaction of all concerned, but in which microscopic proof was lacking. All of these cases occurred in veterans, and none in active service patients. A previous report<sup>4</sup> of cases of this disease from this hospital, covering the 31 month period from January 1, 1937, to August 1, 1939, consisted of 30 proved cases. It is obvious, therefore, that the incidence of the disease in the veterans admitted to the Philadelphia Naval Hospital is increasing. This increase is even greater than it seems, since the number of veterans admitted per year to the hospital during the period included in this report was actually less than during the period of the first report.

*Symptoms and Signs.* There are, unfortunately, no symptoms or physical signs that are pathognomonic of carcinoma of the lung. In this series cough and sputum were the most common symptoms, being present in all but one of the patients. Two other common symptoms, which often were actually responsible for the patient's admission to the hospital, were chest pain, which occurred in 75 per cent of the cases, and hemoptysis, which occurred in 60 per cent. Other symptoms frequently complained of were loss of weight, weakness, shortness of breath, and wheezing or asthma. All of these symptoms obviously could belong to many other chronic lung diseases, as tuberculosis, lung abscess, or bronchiectasis.

Abnormalities on physical examination of the chest were present in all cases, but they too were not pathognomonic, and simulated the findings in other chronic lung diseases. Since bronchogenic carcinoma often produces bronchial stenosis eventually and since most of our patients were first seen relatively late in the disease, signs of atelectasis in the portion of the lung distal to the bronchial occlusion were the most common physical signs suggesting the disease, and were present in 55 per cent of the cases. In 25 per cent of the patients, pleural effusion was present when the patient was first seen.

*Roentgen-Ray Changes.* All of the patients in this series showed abnormalities on chest roentgen-ray. Unquestionably, the chest roentgen-ray



is the first important procedure, after the history and physical examination have been done, in establishing the diagnosis of carcinoma of the lung. It is possible, however, to have a normal chest roentgen-ray in an early case. Four per cent of Overholt and Rumel's<sup>1</sup> series of 75 cases had negative chest roentgen-rays, because the tumor itself was not radiopaque, and because changes in the lung tissue surrounding the tumor had not yet taken place. In a later paper, Overholt<sup>5</sup> has emphasized the importance of routine chest roentgen-rays of men over 40 years in case-finding in lung cancer, comparing its importance to routine chest roentgen-rays of young adults in case-finding in pulmonary tuberculosis.

In this series of cases, the most important roentgen-ray finding suggesting lung cancer was atelectasis distal to the tumor, with accompanying shift of the mediastinum toward the affected side. This occurred in 65 per cent of the patients. Figure 1, the chest roentgenogram of patient S. C. U. taken May 28, 1941, showing partial atelectasis of the right lower lobe, is typical of this group. Bronchoscopic biopsy showed squamous cell carcinoma. Thoracotomy was done on July 28, 1941, but the case was found to be inoperable because of extensive diaphragmatic adhesions. The patient was

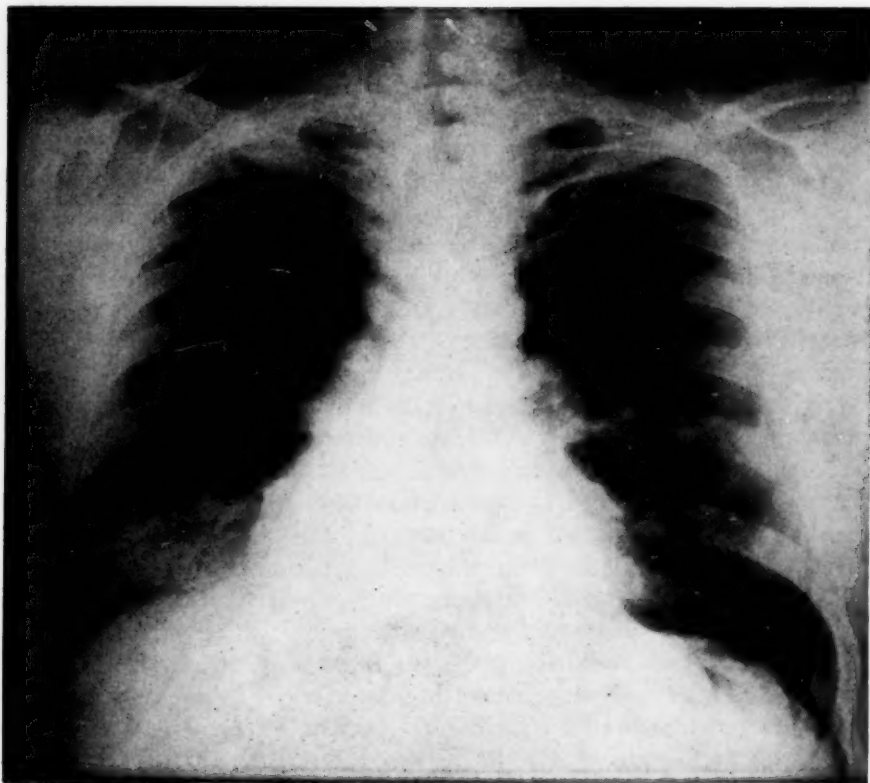


FIG. 1. Chest roentgenogram of S. C. U. taken May 28, 1941, showing partial atelectasis of right lower lobe. Bronchoscopic biopsy showed squamous cell carcinoma.

subsequently given roentgen-ray therapy, and is still alive and in fairly good condition.

Another type of lesion seen by roentgen-ray, less common than the atelectatic type described above, is the single circumscribed lesion, which is usually peripheral and beyond the reach of the bronchoscope. Fifteen per cent of our cases belonged to this group. Figure 2, the chest roentgenogram of pa-

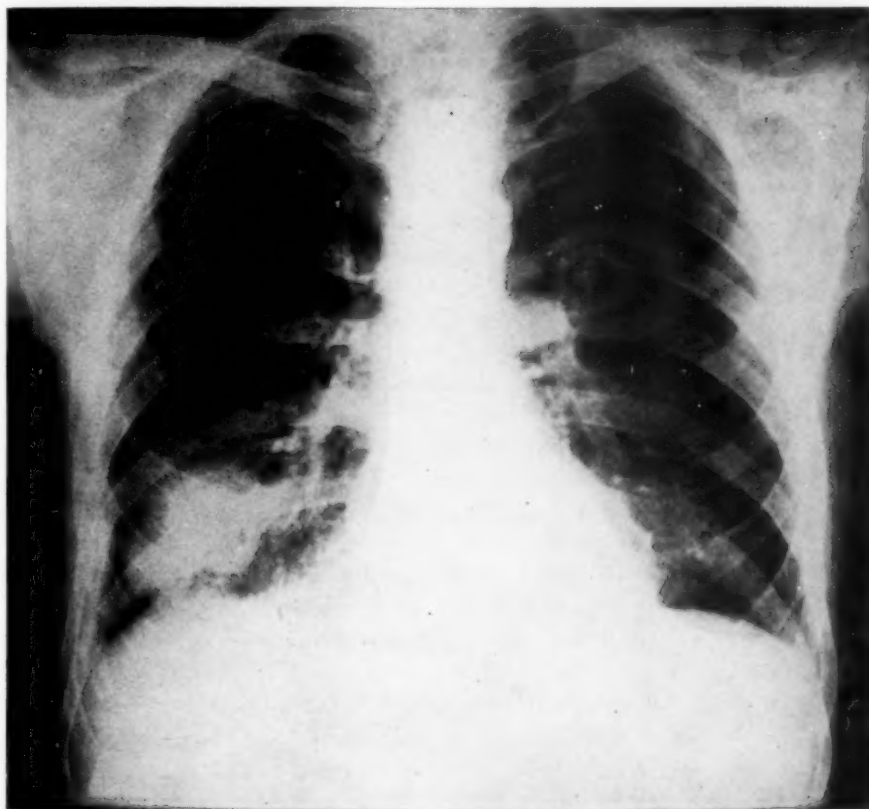


FIG. 2. Chest roentgenogram of J. E. F. taken June 24, 1942, showing a circumscribed lesion in the right lower lobe, proved at autopsy to be adenocarcinoma.

tient J. E. F. taken June 24, 1942, showing a circumscribed lesion in the right lower lobe, is fairly typical of this group. This patient, whose presenting symptoms were such that he was admitted to the neurological service, was too sick during his period of hospitalization to be bronchoscoped. Autopsy showed primary adenocarcinoma of the lung, with metastases to the brain and adrenal glands.

#### METHODS OF ESTABLISHING THE DIAGNOSIS

1. *Bronchoscopic Examination and Biopsy.* This is the most important diagnostic procedure in establishing a positive diagnosis of bronchogenic

carcinoma. About three-quarters of all primary carcinomata of the lung have been found to be within reach of the bronchoscope. Bronchoscopic examination should not be postponed in any suspicious case. In general, the course of the disease is rapid, averaging eight to nine months in untreated cases from onset of symptoms to death, so that a month's delay in establishing the diagnosis by bronchoscopy may make the difference between an operable and an inoperable case. In addition to establishing the diagnosis, bronchoscopic examination often helps determine, by localizing the tumor, whether or not a case is operable, and may also improve a patient's health, by draining a suppurative process distal to the tumor.

Bronchoscopic examinations, often repeated, were done in all but six of the proved cases in this series, and in all of the suspected cases. Biopsies were taken if any abnormal tissue was seen through the bronchoscope. The six cases not bronchoscoped were too ill during their period of hospitalization to tolerate this procedure. Positive bronchoscopic biopsies were obtained in 14 of the patients bronchoscoped, 45 per cent of the proved cases.

2. *Bronchography with Iodized Oil.* This procedure helps to make the diagnosis in a few cases, but is not nearly as valuable as is bronchoscopy. It was used in 12 of our cases. It cannot establish a positive diagnosis by itself, of course. However, when it shows bronchial stenosis proximal to an area of atelectasis in a suspected case, it gives pretty definite proof that a tumor is present, as it did in patient J. C. M. Figure 3 shows this patient's chest roentgenogram taken June 2, 1942, after the installation of lipiodol. A biopsy could not be obtained in three bronchoscopic examinations, because abnormal tissue was not seen through the bronchoscope. This patient has recently died. Autopsy showed primary adenocarcinoma of the lung, with metastases to the bones, brain, liver, and adrenal glands.

3. *Examination of Pleural Fluid for Tumor Cells.* In only one of the 12 cases in which pleural fluid was present was the diagnosis established by finding tumor cells in the fluid. The finding of tumor cells in pleural fluid shows that the case is inoperable, since it means that extension of the tumor to the pleura has already taken place. In fact, it is generally believed that the presence of pleural fluid in a case of lung cancer makes the case inoperable, whether tumor cells are found in it or not.

4. *Examination of Sputum for Tumor Cells.* This procedure has only limited application; it did not establish the diagnosis in any of our cases.

5. *Aspiration Biopsy of the Lung.* This procedure was not used in any of our cases. It is almost universally condemned as being too dangerous because of the possibility of air embolism. Furthermore, as Overholt<sup>5</sup> has pointed out, surgical exploration is indicated in any case in which aspiration biopsy is done, regardless of the outcome. For if the result is positive, the case should be operated upon anyway, and if it is negative, exploration will have to be done to establish the diagnosis.

6. *Exploratory Thoracotomy.* Lung surgeons now believe that in a suspicious case exploratory operation should be performed to establish the

diagnosis and determine operability, provided there is no evidence of metastasis and the patient is in reasonably good health otherwise. In this series, exploratory thoracotomy was the method of establishing the diagnosis in two cases. Unfortunately, both of these patients were found to be inoperable, because of extension of the growth beyond the limits of removability.

7. *Biopsy from a Metastasis.* This was the method of establishing the diagnosis in three of our cases. In one patient, the metastasis was in an



FIG. 3. Chest roentgenogram of J. C. M. taken June 2, 1942, after lipiodol installation, showing stenosis and obstruction of the left lower lobe bronchus proximal to a lesion in the left lower lobe, proved at autopsy to be adenocarcinoma.

axillary lymph node; in one it was in a supraclavicular lymph node; and in the third it was in the subcutaneous tissues of the left upper arm. Cases in whom the diagnosis is established by this method are obviously inoperable.

8. *Autopsy.* This is, of course, the final but certainly least desirable method of establishing the diagnosis in a suspected case. In 11 of our cases the diagnosis was finally established by this method. In all of them, however, the correct antemortem diagnosis of carcinoma of the lung had been made.

Table 1 summarizes the method by which the diagnosis was established in the 31 proved cases.

TABLE I  
Method of Establishing the Diagnosis

Method	Number of Cases	Percentage of Cases
Bronchoscopic biopsy.....	14	45
Necropsy.....	11	35
Biopsy from metastasis.....	3	10
Operation.....	2	7
Tumor cells in pleural fluid.....	1	3
Total.....	31	100

*Microscopic Type.* Of the many classifications of the microscopic appearance of bronchogenic carcinoma, the simplest and most widely used is that which divides them into the differentiated, including squamous cell or epidermoid carcinoma and adenocarcinoma, and the undifferentiated (oat cell carcinoma). Combinations of any two or of all three forms may be present in the same specimen. The squamous cell type is the commonest and, as a rule, the slowest growing. In this series of 31 cases, 16 were squamous cell carcinomata, four were adenocarcinomata, and 11 were undifferentiated or mixed types.

*Treatment.* As in all cancers, two forms of treatment are available, radiation and surgery.

*Radiation Therapy.* There has been a good deal of argument as to the place of roentgen-ray therapy in cancer of the lung. Proponents of roentgen-ray therapy cite the case of a five-year survival after this form of treatment reported by Harper.<sup>6</sup> However, Brock's report<sup>7</sup> of an eight-year survival without any treatment at all makes Harper's case less significant. Overholt and Rumel<sup>1</sup> found that patients who received high voltage roentgen therapy in cancericidal doses lived, on the average, only two-thirds as long as did untreated patients. There is general agreement that roentgen-ray has failed as a curative agent in lung cancer, and that it should be used only as palliative treatment in inoperable cases, to relieve such symptoms as pain or dyspnea. Of the proved cases in this series, roentgen-ray therapy was used in 16 inoperable cases, including four of the six cases in which exploratory thoracotomy had been done. In no case was the patient cured, but in about half there was marked relief of symptoms, and the patients were more comfortable than before treatment.

*Surgical Treatment.* Of our 31 proved cases, seven were considered candidates for exploratory thoracotomy. One of these refused to be operated upon. Unfortunately, all of the other six patients proved inoperable because of extension or metastasis of the lesion, or because of too extensive pleural adhesions. One of these six patients died on the fourth postoperative day. The other five survived the operative period. One of these died 10 months later of cerebral metastases; the other four are still living, 16 months, seven months, one and one-half months, and one month respectively after the



operation. In all of the patients who died and were autopsied, metastases were present, proving the cases inoperable. In the other patients not operated upon, including both the suspected and proved cases, either evidence of metastases was present or other complicating factors such as old age, diabetes, or heart disease, which made the surgeons hesitate to perform such an extensive operation.

*Fate of the Patients in This Series.* Of the 31 proved cases, 16 have died and have been autopsied, six have died and were not autopsied, eight are living, most of them with evidence of metastasis, and one has been lost sight of. Of the 16 unproved cases, four died and were not autopsied, eight are known to be living, most of them with evidence of metastases, and four have been lost sight of.

#### DISCUSSION AND COMMENT

It is generally agreed that surgical removal offers the only hope of cure of carcinoma of the lung. Thoracic surgeons now believe exploratory thoracotomy to be indicated, if an expert is available, in any suspected case of lung cancer, provided there is no evidence of metastasis and the patient is in reasonably good health otherwise. They draw the analogy to exploratory laparotomy in suspected cases of carcinoma of the stomach or colon. The recent report of Overholt<sup>5</sup> shows that exploratory thoracotomy should not be reserved for proved cases. Of 30 suspected cases of lung cancer that he explored, 13 removable malignant lesions were found.

The mortality of the operation in the hands of experienced chest surgeons is rapidly decreasing. For example, Overholt's<sup>1</sup> mortality was 33 1/3 per cent from 1933 to 1936. Since then, he has reduced this to 16 2/3 per cent. The outlook for recovery obviously depends on the skill and experience of the surgeon who is operating. In Overholt's<sup>5</sup> series of 31 pneumonectomies for operable lung cancer, almost half of the patients, 13, were alive and well and free from evidence of recurrence or physical deformity several years after operation; three of these patients had survived more than five years. Graham<sup>8</sup> has one patient living and well nine years after operation, one patient who has remained free of symptoms for six years after operation, two five-year cures, and 20 patients alive and well more than one and one-half years after operation. Graham<sup>8</sup> has emphasized the hopeful aspects of surgery for lung cancer, citing the fact that this type of surgery is further advanced in its first 10 years of life than was surgery for cancer of the colon at the end of its first 10 years. There is no doubt that, in the hands of the real experts in thoracic surgery, such as Graham, Overholt, Rienhoff, Churchill, and others, the outlook for patients with bronchogenic carcinoma is comparatively good, and as more and more men are trained in thoracic surgery, more and more patients will be cured. In the hands of general surgeons, however, the operative mortality of pneumonectomy is high, and most of them, quite rightly, hesitate to attempt the operation.

All in all, the outlook for most of the thousands of patients who develop carcinoma of the lung each year is still far from good. This is shown by the fate of the patients in this series and by the recent report of Perrone and Levinson,<sup>9</sup> who found that operation could be considered in only three of their 77 patients with positive bronchoscopic biopsies. In the great majority of cases, carcinoma of the lung still remains a highly fatal disease for two reasons: (1) the difficulty and delay in establishing the diagnosis; and (2) the technical difficulties involved in surgical removal of the diseased lung even in operable cases. It is up to the general practitioners and internists to appreciate the great frequency of primary lung cancer and to see that, with the aid of roentgenologists and bronchoscopists, cases are diagnosed early and referred for surgery while they are still operable. It is then up to the surgeons to continue the truly remarkable reduction of the operative mortality in pneumonectomy they have already effected and to see that more surgeons, who can maintain this low operative mortality, are trained in this highly difficult and specialized field. I hope and believe that the outlook for these patients will become increasingly better and that carcinoma of the lung will eventually become one of the relatively curable types of cancer.

#### SUMMARY

During the 21 month period between January 1, 1941, and October 1, 1942, there have been 31 proved and 16 suspected cases of carcinoma of the lung among the veterans admitted to the Naval Hospital in Philadelphia.

Of the proved cases, the diagnosis was established by bronchoscopic biopsy in 14 cases, by necropsy in 11 cases, by biopsy from a metastasis in three cases, by exploratory thoracotomy in two cases, and by finding tumor cells in the pleural fluid in one case.

Seven cases were considered candidates for exploratory thoracotomy. One of these refused to be operated upon. All of the other six cases proved to be inoperable. One of these died four days postoperatively, one died of cerebral metastases 10 months after operation, and four are living. The other patients were considered inoperable because of evidence of extension or metastasis, or because of other complicating diseases.

In order to reduce the mortality of this disease, its great frequency must be constantly kept in mind, bronchoscopy must be performed early in suspected cases, and exploratory thoracotomies must be done by men specially trained in thoracic surgery in suspected as well as proved cases without evidence of metastasis.

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## PROBLEMS OF FLUID BALANCE IN THE TRAUMATIZED PATIENT \*

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FROM the standpoint of therapy, body fluids may be considered as composed of water, sodium chloride, glucose, basic ions such as sodium, acid ions such as chloride and the protein and cellular constituents of the blood. There are, of course, numerous other solutes in the plasma such as calcium, magnesium, and potassium chlorides, urea and various phosphates, but with the exception of calcium in certain unusual conditions the need for parenteral administration of these substances has not been demonstrated.

Perhaps the commonest disturbance of fluid balance due to trauma is blood loss as in hemorrhage. In this condition all of the body fluids are lost, but the reduction in blood volume is the serious factor in acute hemorrhage and the reduction in the hemoglobin is apt to be the most serious factor in chronic or repeated hemorrhage.

For this reason it has been shown by Best and Solandt that plasma is extremely satisfactory in the treatment of acute hemorrhage in a previously healthy individual. It should not, however, be used in one who was anemic previous to his hemorrhage nor is it adequate to use again and again in cases of repeated hemorrhage.

Patients with abdominal injuries may require suction drainage; they may develop intestinal obstruction; or they may develop intestinal fistulae. Consequently they may present as complicated problems in fluid balance as any that can be encountered. Furthermore, the traumatized patient may be dehydrated prior to his injury as the result of a lack of water, or a diarrhea due to infection of the intestinal tract. It is impossible, therefore, to segregate the problems of fluid in the traumatized patient from the problems of fluid balance in general.

Imbalance is not always due to a discrepancy between intake and output but may also be due to a shift of fluid within the body. The outstanding example of this is the shift of plasma from the intravascular to the interstitial spaces in patients with burns and in certain other types of traumatic shock. In these cases there is a special and urgent indication for plasma transfusions. This phase of the subject is being presented by Dr. Walter Estell Lee in his paper entitled "The Crush Syndrome and Burns."

The needs of patients with disturbed fluid balance have been recognized qualitatively for a good many years. The investigations of the last few years, however, have emphasized the need for quantitative methods in the correction of these disturbances.

\* Presented October 22, 1942, at a program of Postgraduate Nights arranged by the American College of Physicians at the United States Naval Hospital, Philadelphia.

Although it is true that three liters of physiological saline solution a day may permit the average patient to regain water balance, salt balance, and acid base balance, direct observations on numerous individual patients will show dangerous variations in salt and water retention and in some cases a failure to attain a normal acid base equilibrium.

Fortunately water and salt balance seldom become problems in the acutely traumatized patient for 12 to 24 hours unless the trauma has been preceded by a disturbance such as from excessive perspiration or water deprivation. This interval may allow time for the evacuation of the more complicated cases to areas where the aid of a laboratory is available. During this early period plasma and occasionally whole blood in addition will usually be indicated.

In observations on burn cases at the Pennsylvania Hospital we have been impressed with the fact that the pulse volume and particularly the skin temperature of the extremities were valuable guides in the administration of plasma. In general if the plasma volumes estimated from the hemoconcentration did not fall below 70 per cent of normal, the peripheral circulation was well maintained. In instances in which the peripheral circulation was poor it would, as a rule, become satisfactory when enough plasma had been given by transfusion to restore the plasma volume to 70 per cent of normal. Even without the benefit of hematocrit or hemoglobin determinations it should be possible to gauge the administration of plasma fairly satisfactorily on the basis of the peripheral circulation.

*Estimation of Water Deficits.* In patients who are under continuous observation it is customary to estimate the water deficit by dead reckoning. A certain amount is allowed for insensible loss, and loss by other avenues is measured or estimated.

If patients show signs of dehydration when first seen, however, it is important to realize that an extensive deficit must be assumed. Collier and his associates consider that this usually amounts to 6 per cent of body weight or approximately a gallon and a half for a large man. The deficit may of course be substantially greater than 6 per cent in severe dehydration.

Such an individual, should he have to undergo anesthesia and operation, might require eight to ten liters of fluid during his first 24 hours of hospitalization.

*Estimation of Salt Deficits.* The chloride concentration is most often disturbed in one of two ways. Either there has been excessive loss of salt-containing perspiration which has been replaced by ordinary drinking water, or there has been an excessive loss of gastrointestinal juices compensated by the administration of fluids containing little or no salt. Collier and Maddock's rule of half a gram of salt per kilogram of body weight for a hypochloremia of 100 mg. per 100 c.c. below normal has been very helpful. With severe losses the sodium chloride has sometimes been given intravenously in 2 per cent solution, but in most instances it may be given satisfactorily at the isotonic concentration of 0.85 per cent.



In patients with hypoproteinemia or in dehydrated patients with normal plasma protein concentrations it is unwise to give the full amount of salt at once as such patients may develop peripheral and pulmonary edema.

*Quantitative Correction of Disturbances in Acid Base Balance.* Disturbances due to the formation of ketone bodies either as the result of diabetes or of starvation generally respond well to the administration of glucose and saline solutions (with insulin if indicated). At certain times, however, it is valuable to have a parenteral method of correcting a reduction in the  $\text{CO}_2$  combining power of the plasma rapidly.

In these cases one-sixth molar sodium lactate solution may be employed. One and eight-tenths c.c. per kg. of body weight may be allowed for each one volume per cent change desired in the  $\text{CO}_2$  (Hartmann).

Until recently no clinically tested method has been available for overcoming alkalosis by parenteral means. During the last few months ammonium chloride solutions have been employed for this purpose by Zintel, Rhoads and Ravdin at the Hospital of the University of Pennsylvania. On the average 1.2 gm. of ammonium chloride have resulted in a reduction of one volume per cent in the plasma  $\text{CO}_2$  in a 150 pound person. This is approximately equal to 2 c.c. of sixth molar solution per kg. of body weight.

The trial of this method has been limited and cannot be stated to be of proved safety. No serious reactions have been encountered in the group of patients who received it, however, and it should be considered when alkalosis nephrosis is threatened and when the oral route is not available.

#### SUMMARY

The importance of correcting disturbances in fluid balance as quantitatively as possible is stressed.

Methods of estimating the electrolyte requirements of patients with hypochloremia and with disturbed acid base equilibrium are discussed.

## THE RELATION OF THE CRUSH SYNDROME TO THAT OF BURNS AND OTHER TYPES OF TRAUMATIC WOUNDS OF HUMAN TISSUES \*

By WALTER ESTELL LEE, M.D., *Philadelphia, Pennsylvania*

THE purpose of this paper is to call attention to evidence which is gradually accumulating that such diverse traumatic injuries as (1) *blast*, (2) *burns*, (3) *crush*, and (4) *trauma of the soft tissues* all probably have at least two etiological factors in common: (1) The loss or escape of plasma from the circulating blood stream, and (2) a toxemia resulting from degenerative changes and products liberated from dying or dead tissue cells, plasma and bacteria.

The subject chosen, the relation of the *crush syndrome* to that of *burns* and other *types of traumatic wounds* of human tissues, represents an obsession of ours which is the result of an experience in France during World War I, and which at last has been confirmed experimentally by Blalock and reported in the October 1942 number of *Surgery, Gynecology and Obstetrics*. In this paper he discusses the syndrome of several types of injuries dealing with a conglomeration of reactions to *tissue damage* which, at present, are grouped together under the term *shock*. He suggests it might be wise if the term shock could be abolished altogether, but we agree that common usage makes this impossible at the present time.

No one will question the advances which have been evolved in surgical treatment since the last war and the relatively astounding results now being obtained in the treatment of trauma. In burns alone, before 1914, a hospital mortality of 80 per cent in severe massive, third degree burns was accepted, whereas at the present time reports from the Council of Medical Research show an average mortality in this type of burn of from 7 to 10 per cent.

My theme during these years has been that this gradual lowering of the mortality, decrease in length of hospitalization and lessening of the disfigurement and permanent disability from scar tissue in burns is due to appreciation of the fact that *burns are open traumatic wounds*; and to hear Blalock classify them with hemorrhage, trauma to large masses of muscle, blast, crush injuries and postoperative complications, etc., would seem to justify our teaching.

*Blast.* Little was known about the nature of this injury until the present war and practically all the clinical knowledge we now have about it is based upon reports from the British. Zuckerman and his associates, in 1942, reported in the *Lancet* their experiments with rabbits which were directly ex-

\*Read before the meeting of the Postgraduate Nights of the American College of Physicians held at the Naval Hospital, Philadelphia, October 22, 1942.

posed to high blast pressures (from which their respiratory systems were protected) in which they found abdominal and thoracic lesions caused, they believe, by a wave acting upon the *surface* of the body and not, as previously supposed, by either the pressure or suction components of the wave acting through the nose and mouth. They conclude that both the thoracic and abdominal lesions may be due primarily to the impact of the pressure component on the body wall and that these lesions can occur when the suction component is excluded.

*Immediate death*, unassociated with evidence of external trauma in some instances, may be due to occlusion of the large bronchi by blood clot. *Delayed death* is usually due to pulmonary edema and less often to intraperitoneal hemorrhage. In the reports from their clinical experiences with civilians, however, intrapulmonary hemorrhage of some kind is the most frequent finding, making this one condition in which blood transfusion or blood substitutes are contraindicated whereas morphine and oxygen are required. It would seem then that from the clinical and experimental evidence, injuries to pulmonary tissues by blast may result from direct trauma through the respiratory system or indirectly by pressure upon the body surface.

*Burns.* Our main reference to the problem of burns will be to point out the similarity of the basic tissue damage and tissue reaction to what are now called crush injuries and probably also to blast injuries.

As early as 1931, Underhill and Blalock found that there is an unusual escape of the blood plasma into the perivascular tissues in this type of injury, and Blalock stated that the loss of such relatively large amounts of plasma from the circulation must be an important cause of the decrease of circulating blood volume which is at least the initiating factor in the decline of blood pressure. Following the reduction of blood volume and the increase in blood concentration many vicious derangements in the physiology of the tissues take place: (a) Decreased elimination by the kidneys. (b) Imbalance between intra- and extracellular fluid cell contents. (c) When present over long periods of time the deleterious effects of tissue and plasma decomposition products and of bacterial products must be considered. There is much evidence which seems to support the theory that *toxemia* is an important lethal factor in burns, and Drinker and his associates have recently found experimentally that lymph collected from a burned area exerts a toxic effect when reinjected into the blood stream of either burned or normal patients.

This finding is of peculiar importance, for it provides evidence of the presence of a toxic substance which acts as a common etiological factor in lesions resulting from such apparently diverse and unrelated trauma as blast, burns, and crush, of the soft tissues.

Of all of these four types of trauma the greatest loss of plasma from the circulation occurs in burns, and up to the present time there is no perfect substitute for its replacement. Whole blood does not provide the amount of plasma lost without dangerously increasing the red blood cell concentra-

tion already existing. On the other hand the injection of large amounts of solutions of crystalloids will further increase the loss of plasma by washing it out of the blood stream through the patient's capillary walls, through which this less viscid solution will pass far more freely than will plasma.

Naturally the need for plasma will be governed by its loss, and a simple and accurate method for obtaining this is very desirable. Most of those suggested obtain averages only and are so graded that no harm will result, but all such average formulas fail to provide for the variations which are so frequent in the individual patient.

We admit that the original formula proposed by us is complicated, but by means of a graph recently prepared by Dr. Wolff this difficulty can be overcome so that it should be possible for every surgeon to estimate the total quantity of plasma remaining in the circulating blood in c.c. or expressed in grams of protein.

#### A CHART OF PROTEIN DEFICITS AFTER BURNS

In order to simplify the calculation of protein losses resulting from severe burns, values were calculated from the authors' equation for the average adult with a normal hematocrit reading of 45 per cent cells, and a body weight of 70 kg. (154 lb.). The calculated protein deficit, in grams, was plotted against the assumed hematocrit values for several plasma protein levels as shown in chart 1. Hematocrit values are represented by points on the horizontal base line, plasma protein deficits or equivalent plasma volumes by points on the vertical margins, and plasma protein concentrations by the curves. Therefore, each vertical line in the chart represents a given hematocrit value and each horizontal line a plasma deficit. To read the deficit for a burned patient, take the point at which the vertical line corresponding to the observed hematocrit value intersects the curve corresponding to the estimated plasma protein level, interpolating whenever necessary. The horizontal line from this point to the left margin of the chart indicates the plasma protein deficit in grams, and to the right the equivalent volume of normal plasma. If the weight of the patient differs markedly from 70 kg., for which the calculations were made, the deficit read from the chart must be multiplied by a suitable factor. An example is given on the chart. If only the hematocrit value can be determined, the protein level is assumed as 6.0 to 7.0 gm./100 c.c. during the first 48 hours following the burn, provided the total intake of fluids is restricted to three liters per day. It should be pointed out that large errors may be introduced if the protein level is unknown. In the uncontrolled burn case the protein level may vary between wide limits.

Hemoglobin levels equivalent to each hematocrit value may be substituted on the horizontal axis. This can be done because the chart defines the relationship of hemoconcentration to plasma protein loss caused by severe burns. The chart, however, cannot be used directly for burned cases complicated by hemorrhage, anemia or polycythemia. The anemic individual,

## CALCULATED PLASMA PROTEIN DEFICIT IN SEVERE BURNS

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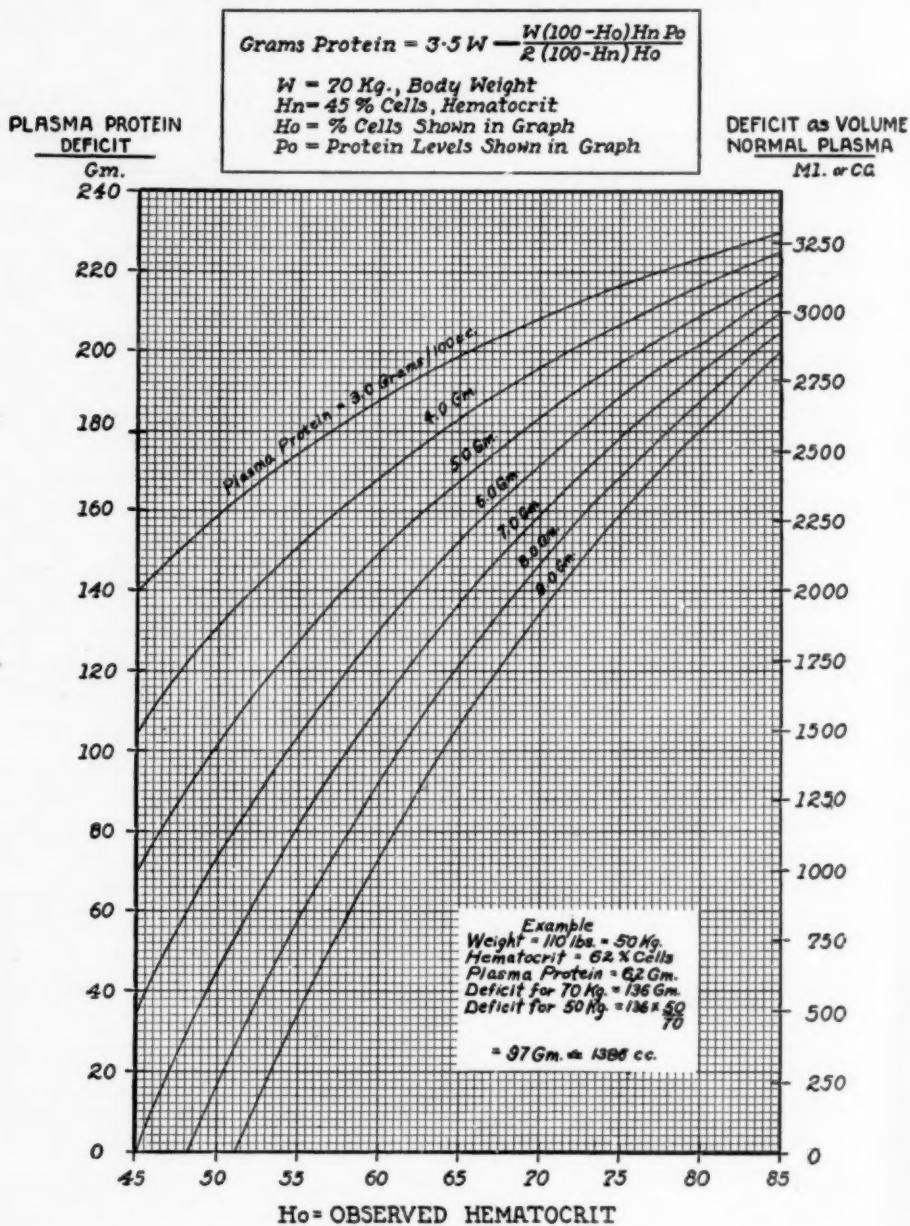


CHART 1.



especially a child, presents a problem not easily handled by any chart or fixed rules. A whole series of charts, one for each basal hematocrit value, is needed for the entire range of anemias. The chart may be used if due allowances are made for the degree of anemia. At the same hematocrit level the plasma deficit for an anemic individual is 20 to 100 per cent greater than that for a person with a normal hematocrit reading. Therefore, values from the chart are minimal and must be increased proportionally for the anemic patient. This is also true for the burned patient who has lost red cells by hemorrhage. In the patient with polycythemia the protein deficit is considerably less than the value indicated by the chart. Allowances must be made for added red cells if a whole-blood transfusion is given. In all of these instances the most dependable value for the protein deficit is obtained by substituting probable normals in the formula and then calculating.

*Crush Injuries.* That there is a relationship—etiologic at least—between the syndromè following crush injuries and those following burns and blast, seems to have been definitely demonstrated, experimentally by Blalock. These three forms of trauma have in common the loss of plasma and the absorption of toxic products resulting from degenerative changes in the tissue cells, and plasma and from bacteria.

Several articles appeared in the German literature before and during the First World War recognizing the tissue effects of crush or compression injuries. It would seem to be chiefly expressed in peculiar renal lesions. This possibility appears to have escaped attention until recently—specifically following air raids upon the British Isles, in persons who have been trapped beneath falling debris. The ischemic muscle, the edema and swelling of the extremities as a result of transudation or escape of plasma, followed by concentration of the blood and terminating in oliguria and uremia expresses a similarity to the phenomena associated with blast and burn injuries. Blalock has been able to produce this condition experimentally in animals by crushing the extremities with a press which exerts a pressure of approximately 500 pounds per square inch. Although there was no immediate change in the general condition of the animal while the press was in action, marked changes occurred within 15 to 30 minutes after its removal. Though they have been unable to reproduce completely the clinical symptoms of the crush syndromè as exhibited by human patients, they do feel that they have evidence at hand that the prolonged ischemia of the extremities which was produced and maintained distal to these pressure points will ultimately end in massive death of tissue. If the presses are removed at the end of five hours and before actual death takes place, there follows an immediate flooding of the general circulation with metabolic products from the ischemic extremity which are probably in some ways similar to the substances of degeneration in the decomposing tissues and plasma and bacterial products of burns and blast and trauma of the soft tissues. Blalock feels it is quite possible that the burn syndromè holds an intermediate position between that of

the trauma alone as in blast of the soft tissues and to the trauma and ischemia which is superimposed in the crush type of wound.

To summarize these four types of injury which are frequently encountered in warfare, the type of the regional and general fluid loss from the general circulation is a constant factor, but the extent may be variable. In addition to this, the degenerative changes of the dead and dying tissue cells, extravasated plasma and the results of bacterial growth and death are to be accepted also as a cause of the toxemia which clinically is found in all three conditions although with varying degrees of severity.

## 35 MM. FILMS IN DIAGNOSIS OF CHEST CONDITIONS \*

By EDMUND C. BOOTS, M.D., F.A.C.P., *Pittsburgh, Pennsylvania*

THE School Health Service Department of the Pittsburgh public schools serves approximately 130,000 children. When only those children were roentgen-rayed who showed enough abnormality to arouse suspicion on observation or physical examination, the standard 14 by 17 film method was sufficient to handle the volume of work.

Two years ago it was decided to make tuberculin testing and roentgen-ray examination of all positive reactors compulsory for all competitive inter-scholastic athletes and ninth grade pupils. When this was done, demand arose for the testing and roentgenological examination of the remainder of the student body whose parents were desirous of having the procedure carried out. As a result of this program, we have tested approximately 40,000 children, have taken 8000 roentgen-rays, and found 44 clinically active cases.

With our limited facilities and personnel, this volume of work could not be done with the standard 14 by 17 films. Therefore, we investigated, observed, and chose the 35 mm. method. We have a 200 milliamper machine and the fluorophotographic attachment using the 35 mm. film. We do not have the services of a roentgen-ray technician.

We use 150 milliamperes, a target distance of four feet, one-tenth second exposure, and vary the kilovoltage according to thickness and type of chest. We have found that it is necessary to give a higher kilovoltage than is indicated on the chart scales furnished with our machine. As the tube ages, these figures have to be increased.

It is our experience that the operator's technic must be more exact with the 35 mm. attachment than with the 14 by 17 films. When a correct technic is secured, the films obtained show as good definition of structure as is obtained with the standard method. In reading these films, they may be mounted individually or read in a roll as we do as a time saving procedure.

A magnifying mechanism is necessary for the reading and several types are in use. There is one view box for use in stereo films, and another projector apparatus which enlarges the image on a screen so that several observers may view the picture at the same time and a pointer can be directed to the image of any desired shadow. We use the direct view box for the roll of flat films, because of the press of time. It is most satisfactory and does not distort the picture. We retake about 4 per cent of the films on 14 by 17 films for conference purposes.

One word of warning: because of the sharpness of detail, abnormalities stand out like a sore thumb when the proper technic has been developed. A

\* Presented before the Fifth Annual Regional Meeting of the American College of Physicians, Philadelphia, Pennsylvania, October 23, 1942.

man not accustomed to reading 35 mm. film is prone to "over read" his films.

This method finds its place where large numbers of films must be taken daily. It is not applicable where only a dozen or so chests are roentgen-rayed in the course of a day. It is of value where film storage space is at a premium. We have 8000 films stored for reference in a space approximately the size of an ordinary file drawer.

This method is recommended for mass survey work. A single film costs less than four cents; a 14 by 17 film would cost 65¢. Using 35 mm. film enables us to take pictures in approximately one-tenth the time and at one-tenth the cost.

The measurement of the cardiac silhouette can be made on these films quite satisfactorily.

We are very well satisfied with this procedure. It has served our purpose well.

## ACUTE NEPHRITIS AND THE EFFECT OF SULFONAMIDES ON THE KIDNEYS \*

By FRANCIS D. MURPHY, M.D., F.A.C.P., and WILBUR D. WOOD, M.D.,  
*Milwaukee, Wisconsin*

THE sulfonamides in their relation to the kidney may play the rôle of the "double-edged sword." They may participate in curing acute glomerulonephritis, or pyelitis, or they may harm the kidneys. Renal damage is considered the most important of the serious complications of sulfonamide therapy. It may result either from obstruction caused by masses of sulfonamide crystals in the renal tubules or ureters, or from parenchymal changes due to the nephrotoxic action of these drugs. Many reports have been published regarding the mechanical blocking of the tubules, pelves and ureters, and the hematuria, oliguria, anuria and uremia which may follow the blocking have been carefully studied.<sup>1, 2, 3, 4, 5, 6</sup> Reports of the nephrotoxic action of sulfonamides have been less common, but it is not improbable that many milder forms of renal damage of this kind have passed unrecognized or, at least, unreported. Enough evidence has been obtained to show that some patients may develop pathologic changes of the kidney in the absence of mechanical obstruction.<sup>1, 4, 5, 7, 8, 9, 10</sup> In some instances both kinds of injury may be found in the same kidney.

The beneficial effects of the sulfonamides in the treatment of acute nephritis are not well known, because of the prevalent fear lest these drugs aggravate the injury of an already diseased kidney. It is known, however, that sulfanilamide is excreted almost entirely in its free form by the kidney, and that the crystals of the acetylated form are not found, as they are with sulfapyridine, sulfathiazole, and sulfadiazine. The report by Williams, Longcope and Janeway<sup>11</sup> suggests that sulfanilamide may play an important rôle in the treatment of acute glomerulonephritis. These authors believe that sulfanilamide may attack the foci of infection which support the activity of nephritis. They found no instance of any injury to the kidney due to sulfanilamide. The use of sulfapyridine, sulfathiazole, and sulfadiazine presents a somewhat different problem because of the insolubility of the acetylated forms of the drug, which are excreted by the kidney and which may cause mechanical interference with renal function.

*Observations on Benefits from Sulfonamides in Treating Patients Who Have Acute Glomerulonephritis.* Our experience with sulfonamides and acute nephritis has been limited to observations on patients who had other diseases than nephritis which called for sulfonamide therapy. In this group

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there were three cases of acute nephritis in which the sulfonamides not only were not harmful, but were beneficial. One of these cases will be reported in some detail, as it is illustrative of our experiences with this group.

Of the three cases, one was a patient with an acute glomerulonephritis resulting from an acute streptococcal sore throat. The nephritis cleared up after giving sulfanilamide for a period of one month by the method usually employed in the administration of this drug. The second case was one of acute lobar pneumonia with an exacerbation of a latent glomerulonephritis. Sulfadiazine was given according to the usual methods. The acute nephritis was not made worse, but improved, and although complete healing of the kidney did not follow, the nephritis again became latent. The third case is the best example of the group and will be given in more detail.

#### CASE REPORT

A 12 year old boy was admitted to the hospital on September 7, 1942 because of fever, vomiting, puffiness of the entire body, and shortness of breath. The boy had been in good health up to four days prior to admission, when chills, fever, and vomiting developed abruptly.

**Physical Examination:** The physical examination revealed a dyspneic, flushed boy with a fever of 105° F. The pulse was rapid, and the apex beat was slightly displaced to the left. There was a lobar pneumonia involving the right lung. Blood pressure was 150 mm. Hg systolic and 110 mm. diastolic. The leukocyte count was 18,500 with 48 per cent nonsegmented neutrophilic cells.

**Urinalysis:** The specific gravity was 1.014. Albumin, four plus. There were many granular casts; 8 to 10 red blood cells and many pus cells per high power field. The urinary output during the first 24 hours was 450 c.c.

The non-protein nitrogen was 68 mg. per cent.

**Treatment:** Two grams of sulfathiazole were given at once, and 1 gram every four hours thereafter for seven days. The sulfathiazole level in the blood ranged during the course of the pneumonia from 8 to 11 mg. per cent. In eight days the pneumonia was brought under control. The leukocyte count and fever dropped almost to normal and the patient was greatly improved. The glomerulonephritis was not intensified; on the other hand, it had subsided somewhat. One gram of sulfathiazole was then given every eight hours for the next five days. The fever at this time began to rise again, and further examinations and roentgenogram of the chest showed the beginning of an empyema. Fluid was removed from the chest and pneumococci were demonstrated in culture. Shortly afterwards closed drainage was established. Sulfathiazole was administered in 1 gram doses every eight hours, and the blood level was maintained between 4 and 8 mg. per cent. The treatment of the empyema and nephritis was continued for six weeks during which time the empyema was cured and the nephritis improved, though it was still active. The patient was treated with sulfathiazole in 1 gram doses every eight hours for another six weeks, and by the end of this period the glomerulonephritis had completely healed.

**Summary of Case:** A boy, 12 years old, developed pneumonia and acute glomerulonephritis in early September, 1942. With the usual doses of sulfathiazole, the pneumonia was controlled in eight days. The acute nephritis was not made worse, but showed some improvement. Subsequently empyema developed. Sulfathiazole was continued along with other treat-

ment for a period of six weeks. The empyema was cured and the acute nephritis made much better. Sulfathiazole was given for the treatment of the acute nephritis for another six weeks, and during this period the acute nephritis was completely cured.

*The Nephrotoxic Action of Sulfathiazole.* The insoluble, acetylated forms of sulfathiazole may produce blocking of the urinary passages followed by albuminuria, hematuria, pain, oliguria, anuria, and uremia. Of the kidney injuries caused by the sulfonamides, this is the commonest, but there is another type of kidney damage that is not characterized by obstructive lesions. By some process not entirely clear, the sulfonamides may impair kidney function by action particularly upon the kidney tubules. Postmortem examinations have disclosed that the glomerular tufts are not involved, and that obstruction by sulfonamide crystals is not the cause. The following is a case that exemplifies renal damage followed by oliguria, anuria, uremia and death caused by sulfathiazole, without evidence of urinary tract blockage at any point.

#### CASE REPORT

A white woman, aged 64, developed an upper respiratory tract infection for which the physician who saw her at home gave 1 gram of sulfathiazole every six hours until 8 gm. in all were given. While at home she developed oliguria. Sulfathiazole was stopped and she was brought to the hospital where she was seen by us for the first time.

The patient was a well developed woman who was in a precomatose state and greatly dehydrated. Many râles were heard throughout both lungs, but otherwise her respiratory system was normal. The output of urine which had been scanty at home, diminished at the hospital, and diuresis failed to take place even though large quantities of fluids and other treatments were given. Urinalysis showed albumin four plus, many red blood cells, very many pus cells, and a few granular casts. The fever was remittent in type and ranged from 99° to 101° F. Blood pressure was 148 mm. Hg systolic and 100 mm. diastolic. The average blood counts showed: White blood cells, 8,500; differential count normal; red blood cells, 3,650,000; hemoglobin, 55 per cent. The non-protein nitrogen and creatinine gradually rose despite usual treatment. Urological examination revealed no urinary tract obstruction. She died of uremia nine days after entrance to the hospital.

*Autopsy:* The heart showed nothing abnormal for a patient in her age group.

The lungs were congested but no pneumonic consolidation was found. The bronchi contained grayish-green mucoid material, and on microscopic examination, the smaller bronchi were surrounded in places by areas of polymorphonuclear infiltration. The bronchioles in some areas were occluded by a semifibrinous material.

Hemorrhagic gastritis and colitis were present.

The right kidney weighed 190 gm., the left 185 gm. There were no specific lesions in the pelves or ureters and no calculi or clumps of crystals were seen. The capsules stripped with ease and the surface of both kidneys was smooth and pale. On cut surface, the cortex was red and stood out in sharp relief against the grayish, anemic appearing medullary portion.

*Microscopic Examination:* On histological examination the glomerular capillaries were congested. The Bowman's capsules seemed normal. The epithelial cells of the convoluted tubules, particularly the distal portions, were swollen, and in places degenerated and undergoing necrosis; some of the tubular lumina appeared occluded by

epithelial cells. The collecting tubules contained brownish material which appeared to obstruct them in places. Throughout the medullary portion and to some degree in the cortex small foci of lymphocytic infiltration were found. Examination for sulfathiazole crystals was made, and many were found in the mucosa of the pelves of both kidneys. The kidney picture was not unlike that seen in nephrosis of the chemical kind.

**Remarks.** This case illustrates several lessons on sulfonamide therapy. First, the promiscuous giving of sulfonamides for comparatively innocent upper respiratory tract infections should be avoided. Secondly, in administering these drugs, the precautions which have been emphasized by those most experienced in their use should be adhered to. For example, in this case the patient was in a state of marked dehydration, and it might have been possible to safeguard the kidneys if an optimal amount of fluid had been given each day with the drug. Thirdly, this case shows that in certain individuals even small doses of sulfathiazole may lead to unfavorable reactions. Finally it must be kept in mind that sulfonamides may not only cause a mechanical obstruction of the urinary tract, but they may exert a more direct nephrotoxic action on the renal parenchyma followed by oliguria, anuria and uremia.

*Prophylaxis and the Effect of the pH of Urine on the Formation of Crystals.* An encouraging feature of most of the reports on kidney injuries from sulfonamide therapy is the confidence which writers place in satisfactory methods for their prevention and control.<sup>1, 12, 14</sup> There are probably several factors which are concerned in the genesis of renal damage from administration of sulfonamide compounds. Safeguarding the kidney may be achieved by the following precautions: (1) An adequate intake of fluid, the hydration of the patient's tissues, and a normal output of urine are probably the most important measures for avoiding kidney injury. General opinion is that 1500 to 2000 c.c. of fluid per day must be taken if adequate urinary output is to be assured. (2) The presence of renal insufficiency or of obstructive uropathies must be evaluated before commencing sulfonamide therapy. (3) Careful observations of the quantity of urine and its appearance on gross examination and the microscopic examination for crystals should be made. The presence of sulfonamide crystals does not mean that kidney damage is at hand and that the drug must be stopped, but it does indicate that much care must be exercised concerning the quantity of the drug given, the optimal level in the blood stream and the volume of urine excreted. (4) Finally several investigators have spoken of the importance of an alkaline urine in the prevention of crystal formation.<sup>1, 3, 13, 15, 16</sup> This idea is not held by all observers, and Thompson, Herrell and Brown,<sup>2</sup> and Finland, Peterson and Goodwin,<sup>10</sup> do not stress the rôles of alkalinity and acidity in the precipitation of crystals in the kidney.

It had become our general impression that when the pH of the urine was kept well on the alkaline side, sulfonamide crystals were diminished in the urine. In order to corroborate this opinion, 50 patients were selected at

CHART I  
Relation of pH of Urine to Crystalluria from Sulfadiazine Therapy

Group 1 pH 4-5			Group 2 pH 5-6			Group 3 pH 6-7			Group 4 pH 7 and over		
pH	Crystals	Blood Levels of Free and Acetylated Drug	pH	Crystals	Blood Levels of Free and Acetylated Drug	pH	Crystals	Blood Levels of Free and Acetylated Drug	pH	Crystals	Blood Levels of Free and Acetylated Drug
4.8	0	(F) 8.9	5.4	0	(F) 10.5 (A) 1.7	6.0	++	(F) 14.7 (A) 1.2	7.0	++	
4.8	0		5.0	++	(F) 12.8 (A) 0.82	6.0	+	(F) 14.7 (A) 1.2	7.2	+	
4.9	0	(F) 7.7	5.3	+	(F) 9.6 (A) 2.5	6.4	0	(F) 8.1 (A) 3.2	7.0	0	(F) 5.9 (A) 2.0
4.9	+++		5.3	0	(F) 15.0 (A) 1.36	6.1	0	(F) 8.7 (A) 0.8	7.9	0	(F) 9.6 (A) 1.9
4.9	0		5.8	0	(F) 18.2 (A) 2.6	6.1	0	(F) 10.9	7.5	0	(F) 14.09 (A) 3.5
4.8	0		5.0	+	(F) 11.2 (A) 0.68	6.0	0	(F) 11.75 (A) 1.2	8.6	0	(F) 14.1 (A) 2.8
4.9	+		5.6	+	(F) 10.2 (A) 1.8	6.3	++	(F) 11.9 (A) 0.6	8.2	0	(F) 6.4 (A) 0.6
4.8	++++	(F) 10.2 (A) 0.7	5.1	++	(F) 11.0 (A) 0.8	6.5	+	(F) 12.8 (A) 1.2	7.7	0	(F) 9.5
4.9	++++	(F) 8.1 (A) 1.4	5.5	+	(F) 8.9 (A) 3.6	6.0	++	(F) 11.2 (A) 1.6	7.6	0	(F) 16.3 (A) 3.3
4.9	++++		5.2	+	(F) 13.1 (A) 3.3	6.2	0	(F) 14.6 (A) 0.9	7.6	0	(F) 13.0 (A) 3.0
4.9	+	(F) 8.9 (A) 3.5	5.3	+	(F) 6.3 (A) 1.0	6.7	0	(F) 9.8 (A) 1.5	7.5	0	(F) 12.6
4.8	++++	(F) 7.8	5.3	++++	(F) 8.4 (A) 0.6	6.4	+	(F) 7.8 (A) 1.7	7.6	0	(F) 11.31 (A) 1.3
4.3	+	(F) 8.3 (A) 1.3	5.4	0	(F) 8.1 (A) 0.7	6.0	++++	(F) 10.3 (A) 3.4	7.7	0	(F) 6.9 (A) 2.06
4.8	+		5.4	++++	(F) 9.9 (A) 3.6	6.0	++	(F) 14.5 (A) 2.2	7.0	+	(F) 9.6 (A) 1.2

F—Free drug.

A—Acetylated form of drug.

In group 1 there were 14 urinalyses taken in all, in group 2 there were 88, in group 3, 88 and in group 4, 43. The figures given above are typical of the trend of crystalluria in relation to pH. Averages taken for each group show that alkalinity probably has an effect on the crystalluria. The averages of the crystalluria in each of the 4 groups are as follows: (a) In group 1 with a pH of 4-5, the average number of crystals was 1.642. (b) In group 2, pH 5-6, it was 1.25. (c) In group 3, pH 6-7, the incidence of crystals was 1.022, (c) and in group 4, pH of 7 and over, the average number of crystals was only 0.232.

random and placed on 1 gram of sulfadiazine every four hours. Most of these patients were relatively young and were not afflicted with any kidney or liver disease. Specimens of urine were taken each morning at 10 o'clock and examined within 20 minutes for crystals. The urine was made alkaline by giving soda bicarbonate 1 gram with each gram of the sulfadiazine. The fluid intake was maintained at 2500 c.c. a day, and levels of the free and acetylated drug in the blood were determined every other day. From the findings given in chart 1, it seems that in alkaline urines fewer crystals were found than in those with an acid reaction.

#### SUMMARY

1. Sulfonamides may in some cases cure acute glomerulonephritis, and other acute inflammatory lesions of the kidneys, but under certain circumstances they may cause kidney damage.
2. Two cases of nephritis benefited by sulfonamide therapy are mentioned and a third case described more fully in which treatment with sulfathiazole resulted in complete recovery.
3. A case illustrative of the nephrotoxic action of sulfathiazole is given, and the findings at autopsy are reported.
4. Precautionary measures which have proved their value in cases treated with the sulfonamides are outlined.
5. There is no unanimity of opinion concerning the rôle of alkalinization in preventing crystalluria. A preliminary report of our observations on this question is included. It appears that alkalinity may diminish the incidence of crystalluria.

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## MEDICAL ASPECTS OF HIGH ALTITUDE FLIGHT\*

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SINCE civilization moved north from the warm climates of the southeastern Mediterranean, man has been required to devote some part of his energies to adjusting himself to his physical environment. Historians wish to emphasize that man's migration into new environments is but an expression of progress, and tell us that the restless spirit finds its greatest examples among the hearty of a race who seek "new worlds to conquer." Be that as it may, certainly in recent times many men have not been content with conquering the surface of the earth, but have directed their energies to mastering that which is below and above the surface of the earth.

The history of man shows that he has been ever seeking new means of transportation for the purpose of increasing his speed and for exploring beyond his environment, and each new development in transportation has brought with it its own peculiar medical problems. Travel by water brought with it drowning; the subjugation of animals, fractures of various kinds; the development of the steam engine, the so-called "railroad spine"; the gasoline engine, carbon monoxide poisoning; and with the automobile, the typical Colles fracture. And now we have the air plane with its tremendous speeds, in three dimensions, which introduces entirely new medical problems, as man is now placed in an environment in which he is not naturally adjusted to live. From the time he leaves the ground until he returns, he is living under unnatural conditions. In attaining altitude and traveling at such tremendous speeds he is defying nature.

Some 20 years ago it was realized by a few individuals that the performance of the aeroplane was limited only by the performance of man in this strange environment in which he found himself. The pilot of the aeroplane is the heart and brains of the machine. The machine may be defective, but the pilot brings it to earth. But when the pilot fails only momentarily, no matter how well the machine is functioning, there is no direction to the flight and it crashes. And so to insure the proper functioning of man in this new and strange environment, Aviation Medicine was born, and with it the Flight Surgeon.

We who are intimately connected with Aviation Medicine like to visualize the Flight Surgeon as having the same relation to flying personnel as the engineer has to flying materiel. The engineer assures himself that the machine is functioning perfectly before he allows it to take off into the air. The Flight Surgeon assures himself that the personnel who are to operate the machine will function perfectly.

\*Delivered before the New England Regional Meeting of the American College of Physicians, Boston, Mass., February 5, 1943.

With these preliminary remarks, I would like to call to your attention a few of the medical problems involved in aviation. Aviation, as we know it, involves two big factors: first, the development of the mechanical means of making flight possible; and secondly, the adjusting of the operators or occupants of this mechanical means to the conditions they will face in the environment into which they will be carried.

In regard to the first factor, suffice it to say that the development of the aeroplane has outstripped the development of our knowledge of human beings under conditions of flight. The situation would not be so tragic if aeroplanes were used solely for commercial purposes, but military needs and uses demand high-altitude flying, dive-bombing operations and rapid maneuvering where judgment, split-second reactions, and the effects of acceleration and anoxia are determining factors. Inasmuch as we have not been able to develop a superior race or immunize our flying personnel from the precariousness of operational flying, future gains in flying will of necessity have to be made through advancements in knowledge of physiology and allied subjects.

I would like to outline briefly a few of the main problems in Aviation Medicine with which we are concerned. I will restrict my remarks to five major problems, and give them in the order of their importance:

1. Selection and training of flying personnel.
2. Anoxia or oxygen-want.
3. Aero-embolism.
4. Expansion of gases in the body cavity and alimentary canal.
5. Low temperatures.

It is interesting to note in passing that in the development of aero-medicine, these problems appeared historically about in their present order of importance, and each has been greatly emphasized by the present war. It was my interesting experience to visit England after the battle of Britain to study the findings of the R.A.F., and I have now just returned from Africa. I believe that much of the mastery of the air in the battle areas is dependent upon solving these problems.

*Selection and Training of Flying Personnel.* During the early days of aviation, the selection and training of flying personnel were predominantly on the basis of trial and error, or survival of the fittest. Personnel was not selected because of any peculiar fitness for flying—it was simply a question of whether the individual had the nerve to fly. The result was that the average aviator had a very short time of usefulness. Little by little the physical and mental requirements for entering flying training have been raised, and with the newer methods of selection of trainees, we are speedily removing that costly procedure of survival of the fittest. An extensive program has been established not only to select those aviation cadets who are best qualified to receive flying training, but also to select those for further specialized training and assignment to high altitude operations. This high

altitude training also adequately indoctrinates all members of the air crew in the general subject of high altitude flying. The aero-physician has played a large part in the establishment of this program, and at the present time we have two large research centers and many additional research activities working toward the solution of this problem. The preparation of the flight crew has been almost entirely a duty of the flight surgeon who examines, instructs, and frequently flies with his men. Because of the fact that the selection and training of flying personnel is a separate subject unto itself, I do not believe that it would be wise to do more than to bring it to your attention now. Therefore, I will pass on to the second heading.

*Anoxia or Oxygen-Want.* Aviation medicine requires knowledge of many physical principles which are intimately connected with problems presented in this talk. The question of anoxemia is an excellent example of this. The decrease in barometric pressure which occurs as one ascends to greater and greater altitudes restricts the level to which one can fly without supplemental oxygen, and even the level to which one can fly breathing 100 per cent oxygen. This latter ceiling, as determined experimentally, is approximately 40 to 42,000 feet. Beyond this, pressure cabins or pressure suits must be used. One of our major problems has been that of designing a satisfactory oxygen mask. Our mask today only basically resembles that which we used two years ago. Even were this aspect of the question successfully solved, there remains the fundamental problem of the effect of chronic anoxia upon flying personnel. Although we know that oxygen-want does not have the same effect upon all individuals, we believe that it is mandatory that everyone use oxygen equipment above 10,000 feet, in the event that flight is to be longer than two hours. The individual should never exceed 15,000 feet even momentarily without oxygen, in spite of the fact that he is relatively inactive and has no obvious symptoms. Provided there is a need for a peculiar mental or physical exertion, oxygen should be taken at a lower altitude. The average individual begins to become anoxic at altitudes above 33,000 feet, even though he is breathing 100 per cent oxygen and is engaging in little or no activity. This anoxemia becomes progressively greater with increased altitude. Although it is theoretically possible for a normal individual to ascend to altitudes of about 46,000 feet, it is felt that for military purposes the maximum that should be demanded is 42,000 feet. As a matter of fact, from a medical standpoint, it is desirable to use a pressure cabin for all altitudes above 30,000 feet. At altitudes as low as 4,000 feet, there is commonly a change in pulse rate and a slight rise in blood pressure, which shows a general rise to 8,000-12,000 feet, and then commonly begins to fall.

As a result of the work done by Schneider, it was found that there are two general types of reactors, "fainters" and "non-fainters," which are nearly equally divided. The fainting type are those in whom the lower nervous centers which control the heart rate, vascular tone and volume of

breathing, suffer paralysis before the higher or psychic centers are affected. This fainting type of reactor usually suffers a sudden reduction in his blood pressure at the time of fainting. This general type of fainting reaction should not be confused with the unconsciousness that occurs at high altitudes as a result of a sudden interruption in the oxygen supply system. It should be remembered that the higher the altitude, the shorter the time necessary to produce unconsciousness due to lack of oxygen.

Perhaps the most dramatic demonstration witnessed by research workers using the "altitude training" or "low pressure chamber" is the speed with which unconsciousness overtakes man at altitudes above 30,000 feet. At 35,000 feet without oxygen, unconsciousness will appear in 30 to 60 seconds; at 40,000 feet, in 15 seconds. Above these levels there is progressive acceleration in the appearance of unconsciousness.

*Aeroembolism.* The rapid climbing abilities of modern airplanes have created a situation in which the body of the aviator is rapidly decompressed with danger of liberation of bubbles of gas, mainly nitrogen, from the blood and tissues. This condition in aviators corresponds to the compressed-air illness in deep-sea diving called the "bends." Aeroembolism is a condition caused by the same general process that causes compressed-air illness, with the exception that the former occurs from compression to two or more atmospheres followed by decompression, whereas the latter occurs from decompression from one atmosphere or less.

During ascent in aircraft or in any other situation in which the atmospheric pressure is decreased, the internal partial pressure of the body nitrogen is above that of the nitrogen in the lungs, and the tissues, therefore, are supersaturated. As a consequence, the nitrogen dissolved in the blood begins to be liberated in the lungs. The nitrogen in the tissues begins to enter the blood stream, and by this dual process the body tends to rid itself of its excess nitrogen. If the ascent is slow enough so that the nitrogen in the body can be eliminated before reaching approximately double its normal saturation at the prevailing altitude, nothing unusual will occur. If, on the other hand, concentrations of nitrogen in the body become more than double their normal saturation values at any altitude pressure, the nitrogen will tend to come out of solution and form bubbles.

Since the elimination of nitrogen from the body is entirely through the blood stream, those parts of the body or those tissues which have the poorest blood supply will be least able to lose their excess nitrogen rapidly. That this is actually correct is indicated by the fact that with rapidly decreased atmospheric pressure, these bubbles are found in the spinal fluid and about the spinal column at 18,000 feet, whereas bubbles in the blood and body tissues generally have not been found below 30,000 feet. This entirely agrees with the actual findings in flight where it is not unusual to have minor symptoms, such as itching and tingling sensations, a little above 18,000 feet. It is quite unusual, however, to have an individual incapacitated as a result of aeroembolism below 30,000 feet.



It is obvious that if one ascends slowly enough to high altitudes, the nitrogen of the body will be eliminated as fast as it tends to become excessive. Therefore, the rate of ascent is important since the nitrogen content of the tissue must reach a value at least twice normal at any given atmospheric pressure before it will appear as bubbles.

The calculated maximum rate of ascent which will avoid bubble formation is not more than 78 feet per minute. It is obvious that this rate will always be exceeded in aircraft, and therefore some other solution must be found.

A large amount of information is being accumulated on the preliminary use of oxygen to wash out excess nitrogen prior to take-off. It is known that breathing 100 per cent oxygen for one-half hour, while taking active exercise, will remove a certain amount of nitrogen and will make certain individuals more comfortable during rapid ascents. This procedure, of course, is quite impractical for defensive military operations, and there is still some question as to how much it contributes other than delaying the onset of aeroembolism.

The number of individuals who will be incapacitated at any given altitude is not precisely known. Certain individuals with no preliminary preparation are able to go to 40,000 feet, and above, repeatedly, for one to two hours with no symptoms, whereas others consistently have symptoms which are incapacitating at slightly above 30,000 feet. As a result of the English experience, it is probable that not over one-half of the young, healthy aviation cadets can go to 35,000 feet for four hours without symptoms.

*Expansion of Gases in the Body Cavities and the Alimentary Canal.* Probably one of the most frequent difficulties experienced by flying personnel in flight is with reference to the middle ear. If for any reason the eustachian tube is closed, which may occur during a common cold, pharyngitis or sinusitis, the middle ear cannot be ventilated and a marked change of altitude may then rupture the eardrum. A like condition occurs in the case of the sinuses when their openings are blocked, in which case, during a change of altitude, marked trauma and severe pain may develop. The abdominal distention which occurs as a result of the expansion of gases in the gastrointestinal tract is often severe enough to incapacitate the individual, provided the rates of ascent are rapid.

*Low Temperatures.* The problem of cold or low temperatures was intentionally placed last because it is primarily an engineering problem, and I understand that we are already well on the way to an adequate solution.

*Other Subjects.* I would like to mention briefly high accelerations, fatigue, and clothing, as subjects which have intentionally been omitted from this discussion. Although these subjects are also important and may limit high altitude flights, they are in no way peculiar to such operations and are entirely secondary to the subjects discussed above. The problem of high accelerations will be a greater problem for low-flying aircraft. Fatigue is

not limited to high altitude, although there is considerable evidence that it does develop more rapidly under such conditions. Clothing, although important, is again not a satisfactory answer to the cold problem. Clothing, in general, is entirely inadequate for continued operations if the temperatures are below 10° F.

There is perhaps no one problem of greater importance to the winning of this war than that of the proper application of aviation medicine. It finds its way into every air activity—transport, reconnaissance, and fighting. The reports that I have of recent endeavors toward solving our problems are extremely encouraging. Much work is yet to be done, but American ingenuity and American medical research will solve it.

## THE PRESENT STATUS OF CLINICAL ELECTROENCEPHALOGRAPHY \*

By FREDERIC A. GIBBS, M.D., *Boston, Massachusetts*

AFTER eight years of trial, clinical electroencephalography has gained widespread acceptance. It is being used by neurologists, brain surgeons, psychiatrists, and pediatricians, as an aid in the diagnosis of epilepsy and related disorders and as a painless and entirely safe method of detecting localized damage in the cerebral cortex. Several Army induction centers are using it as part of the medical examination to determine fitness for military service.

This widespread acceptance has placed a burden on electroencephalographic standards for diagnosis and prognosis, and various weaknesses have appeared. In the effort to correct these weaknesses, electroencephalographers in this country and abroad are collecting large numbers of electroencephalograms on normal and abnormal persons at various age levels so that standards can be given a solid statistical basis. Such studies could not be done at an earlier stage because, like most new sciences, electroencephalography in its beginnings was descriptive. Single cases or small groups yielded essential information that revealed the general shape of the field, and provided clues to the directions in which large scale studies could profitably proceed. However, the descriptive stage of clinical electroencephalography is now over; it is entering its quantitative, or statistical phase. This will seem to many a less interesting period, but only in this phase can electroencephalography be rationally applied, for until standards are based on large numbers of uniformly classified cases, electroencephalographic diagnosis will be unreliable.

The study of 1,000 normals and 1,200 epileptics<sup>1</sup> reveals that although some supposedly normal persons show abnormalities of the type encountered in epileptics, certain disorders are so common in epileptics and so rare in normals that they have diagnostic value. For example, the most characteristic type of disorder, namely, seizure-discharges, was observed in 30 per cent of the epileptics and in fewer than 1 per cent of the controls. A somewhat less extreme form of abnormality, very slow or very fast activity, occurred in 25 per cent of the epileptics and in only 2 per cent of the controls. The mildest form of abnormality, moderately slow or fast activity, was twice as common in the epileptics as in the controls. Only 15 per cent of the adult epileptics and 10 per cent of epileptic children were classified as normal, in contrast to 85 per cent classified as normal in the control group, but

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it is clear that a significant proportion of epileptics have normal electroencephalograms in their interseizure periods. Therefore, like a negative Wassermann, a "negative" electroencephalogram is only suggestive. For that matter, a "positive" electroencephalogram is only suggestive. However, it may be *highly* suggestive. The ratio of epileptics with seizure-discharges to normals with seizure-discharges is of the order of 30 to one; therefore, seizure-discharges can be considered confirmatory of epilepsy. Although less significant, very slow or very fast activity is suggestive of epilepsy and such a finding would strengthen a clinical diagnosis of epilepsy. The finding of moderately slow or fast activity is inconclusive, but it is entirely in accord with a clinical diagnosis of epilepsy. If a normal electroencephalogram is reported in a clinical epileptic, it is probably wise to reconsider the grounds on which the diagnosis was made, but if these are found to be satisfactory, there is no reason to doubt the diagnosis.

Much emphasis is placed on epilepsy because that is the condition which presents the widest range of electroencephalographic abnormalities. However, in brain trauma, very evident disturbances of the electroencephalogram are also encountered. Statistically significant data on this condition have been made available by the publication of Williams' study on 600 consecutive cases of head injury at the Military Hospital in Oxford.<sup>2</sup>

Other conditions in which electroencephalography has been found to be clinically useful are the following: cerebral tumor, subdural hematoma, cerebral hemorrhage, cerebral thrombosis, cerebral abscess, meningitis, encephalitis, Schilder's encephalomyelitis, Sydenham's chorea and behavior disorders. It has almost no clinical value in schizophrenia, manic-depressive psychosis, feeble-mindedness, migraine, psychoneurosis and hysteria.

Because so little abnormality is seen in feeble-mindedness or schizophrenia, it is apparent that the electroencephalogram does not give a record of all brain activity. The electroencephalogram records one particular type of brain activity from a particular brain area, namely, the outer convexity of the hemispheres. The electroencephalogram can localize disorder in cortical areas that are otherwise silent, but it does not indicate the cause of the disorder. It supports or weakens a clinical diagnosis, but it does not make a clinical diagnosis. As a source of additional evidence, it may be extremely valuable but it cannot be regarded as a "time-saver."

The value of an electroencephalogram is directly proportional to the experience and ability of the electroencephalographer who makes and interprets it. The taking of satisfactory records requires training and more than common skill and diligence, and their interpretation requires inherent powers of discrimination. However, a primary requirement is that the electroencephalographer be equipped with a correctly designed and properly built instrument. It is impossible for a good man to obtain satisfactory results with a poor instrument, and an incompetent man with a poor instrument is a source of egregious error.

One of the surprising and encouraging aspects of medical practice in this country is the readiness with which innovation is accepted. New and highly technical diagnostic methods become standard procedures almost overnight. In a few more years the electroencephalograph will not be curious or wonderful, but only familiar and increasingly useful.

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## OBSERVATIONS ON IMMUNITY IN MUMPS\*

By JOHN F. ENDERS, PH.D., *Boston, Massachusetts*

THE importance of the problems of the control and prevention of mumps among military personnel was illuminated by the events of the last war when nearly four million man days were lost from duty because of this disease. Wesselhoeft and Walcott<sup>1</sup> recently, in an excellent review, have reemphasized the rôle which epidemic parotitis can play in interfering seriously with the training and movements of troops and have clearly defined the *lacunae* in our knowledge and our technic which have rendered prevention and control unsatisfactory.

Of these deficiencies perhaps that most keenly felt is the lack of a simple method analogous to the Schick test for determining susceptibility or resistance to infection since on epidemiologic grounds it is highly probable that many individuals who have never experienced an overt attack are nevertheless immune. Were such a method available, it is obvious that during an outbreak a considerable number of contacts who, under present conditions, may be subjected to quarantine for several weeks could be safely disregarded. Moreover, in dealing with epidemics it would be possible by this means to check the statement of an individual giving a positive history, as it is well known that the history of mumps may often be unreliable.

Directly related to the problem of establishing a test for susceptibility are the obviously practical questions of the assay of the prophylactic properties of convalescent or normal human serum and of any vaccine which in the future may be devised. For it is evident that if, in a group subjected to study, a significant number of persons are naturally immune who never had recognized mumps, the evaluation of specific prophylactics would be rendered extremely difficult and prolonged in the absence of a means whereby such individuals could be distinguished.

With these considerations in mind, we first undertook the study of one of the reactions of immunity in the rhesus monkey—an animal which Johnson and Goodpasture<sup>2</sup> in 1934 had shown to be susceptible to the virus. The information thus obtained was applied to an analysis of the course of events in the disease in human beings and then to the investigation of the immunologic status of normal individuals.

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A part of the work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the President and Fellows of Harvard College.

The data supporting the statements made in this paper will be recorded in detail in subsequent communications. A preliminary report on the development of complement-fixing antibodies in infected monkeys and in human beings with mumps has been published (*Proc. Soc. Exper. Biol. and Med.*, 1942, 1, 180-184).

We employed the method of inoculation of Johnson and Goodpasture and noted a disease resembling mumps in all important aspects following the instillation of saliva from cases of epidemic parotitis into the salivary ducts of monkeys. In these animals nine serial passages of the virus have been maintained without apparent alteration in its properties by the inoculation of an emulsion of the infected parotid gland removed surgically during the acute phase of the disease. From the operation, recovery is nearly always uneventful.

Since monkeys convalescent from mumps are refractory to reinoculation of the virus, we naturally sought a way of determining whether this immunity might be correlated with the appearance of antibody in the blood serum. For this purpose, the complement fixation test was used in which the antigen consisted of a dilute suspension in saline of the infected parotid gland. As a control a suspension of gland from a normal monkey was regularly included. By this procedure sera of monkeys before inoculation, at the height of the disease, during convalescence and at varying periods thereafter were tested for the presence of antibody. None was detected in the specimens from normal animals or in those taken during the early acute stage. Within three days following the acute stage, however, some antibody was demonstrated and after five days the titer was shown to be high. For a month or somewhat longer this high level was maintained. Gradually the concentration of antibody decreased until amounts comparable to those found in certain normal human beings were reached. The titer then appeared to remain constant for at least 10 months. This persistence of antibody at a low level following recovery is important in relation to the significance of the results obtained in man.

From these data we may conclude, then, that infection of the rhesus monkey with the virus of mumps leads in a short time to the appearance of specific complement fixing antibodies which are not present in normal susceptible animals. Moreover these antibodies may persist in the blood for many months.

By the same procedure sera obtained from mumps patients at comparable periods of the disease have been investigated. Results analogous to those noted in the experiments with animals have been recorded. No antibody was demonstrated in the sera of 10 of 11 cases of typical mumps taken on the first or second day of the disease. It is possible that the patient representing the single exception was ill prior to the recorded time of onset. In five patients when the specimens were first secured on the third to the sixth day of illness, antibody in relatively low titer was found. In these cases, however, as well as in those in which no antibody was initially present, a pronounced increase in antibody concentration has always been subsequently observed. In only one patient have we information concerning a drop in titer from the high level of early convalescence during the following months. But here, at least, the course of events was similar to that in the monkey, since the con-

valescent titer fell within seven months to a level comparable to that found in many normal individuals.

A few tests on sera obtained during and after other infections such as influenza-like disease, German measles and scarlet fever have failed to reveal emergence or increase in antibody reacting with the virus of mumps.

Thus it would appear that in man as in the monkey specific complement fixing antibody is usually absent in the earliest stage of the clinical disease, appears shortly thereafter, increases markedly in amount, and then decreases to persist for at least some months following recovery.

These observations have led to the application of the test as an aid in the diagnosis of cases of encephalitis without definite parotitis, suspected, on clinical grounds, of being attributable to infection with the virus of mumps. In two of six such cases a significant rise in titer has been recorded; and in one of these two no antibody was demonstrated in the specimen taken three days after the onset. It is possible that our failure to demonstrate a rise in titer in every instance may be explained by assuming that encephalitis is a relatively late complication of the infection.

In the six encephalitic patients whom we have studied, however, and in whom the clinician suspected mumps virus as the etiologic agent, titers were obtained which were higher than all but one of the normal human sera we have evaluated. Thus we may suggest that in cases of suspected mumps encephalitis without parotitis the complement fixation test should be helpful in confirming the diagnosis.

In the light of all the foregoing findings, it became of great interest to ascertain whether the complement fixing antibody was present or absent in the sera of normal individuals of varying ages, since its presence might tentatively be taken to denote previous infection with the virus whether or not this had led to clinically apparent disease. Conversely its absence might be assumed to indicate susceptibility.

We have thus far tested the sera of about 265 adults and 115 children. Since in each category many of the histories were unreliable, I will here present only the results of studies carried out on a group of 163 individuals at the Harvard Medical School comprised mostly of male students but including older people as well, together with a small group of 31 normal children three to five years of age attending two day nurseries directed by officials of the Health Department of Boston.

The survey on the personnel at the Medical School revealed the following facts. Antibody occurred in about 92 per cent of the sera of those giving a positive history of mumps. In sharp contrast, 50 per cent of the sera of those who denied having had the disease contained antibody.

It is possible, then, to assume with some confidence that nearly half those individuals who gave reliable denials of having had mumps, at some time underwent an inapparent or "silent" infection which, in view of the solid and persistent immunity usually conferred by the disease, should render them in-

susceptible. On the other hand, the assumption seems justifiable that most of those in whose sera antibody could not be demonstrated did not experience an infection and are therefore potentially susceptible.

The experiments with the children yielded additional data of the same sort. As one would expect in this age group, the percentage of negative reactors with negative histories was greater.

From the standpoint of routine testing of sera, the complement fixation test is laborious and time-consuming. With the possibility in mind of the need for studying large groups of individuals, we sought for another reaction of immunity which might be more simply elicited.

It had been noted that the antigen used in the complement fixation test was still able to fix complement after heating for 20 minutes at 65° C. Under these conditions, however, the infective properties of the virus would presumably be destroyed. Because of the fact that heated mumps virus still was capable of reacting with antibody, and because it has been shown that when inactivated by heat the viruses of vaccinia and lymphogranuloma venereum will still elicit skin reactions in those who have previously been infected with active virus, we carried out a series of experiments in which the diluted heat inactivated suspension of infected monkey parotid was injected intradermally in certain of the normal individuals studied for complement fixing antibody. Included as a control was a heated suspension of normal monkey parotid.

At the site of the injection of the infected parotid suspension, in nearly 100 per cent of those giving a history of mumps, an erythematous reaction occurred after 24 to 48 hours, varying from 1 to 4 cm. in diameter and often slightly indurated. Only a negligible number of reactions occurred at the site of injection of the normal gland material. The reactions usually disappeared within one to four days following the fastigium. As with the tests for antibody, the group giving no history of mumps revealed about equal numbers of negative and positive reactors. Indeed there was evident a close parallelism between the two tests. The skin test, however, was positive in those few cases in which a history of mumps was given and the complement fixation test was negative, a fact which suggests that the skin test may be a more delicate indicator of past infection. In only one child with negative history, the reverse was observed: a negative skin test with positive complement fixation. But it should be stated that in a group of abnormal children in a home for the feeble-minded, a higher percentage of reversals of this sort were observed.

Although the number of individuals in whom both tests have been applied simultaneously is small, we believe that the results so far obtained strongly imply that a positive skin reaction indicates a previous infection with the virus whereas failure to react signifies in most instances potential susceptibility.

As an additional bit of evidence in respect to the specificity of the skin reaction, it can be said that in two patients it has been shown that the skin

test was negative during the acute phase and became positive during convalescence.

Finally, it is clear that the exact significance of these findings can only be determined by extensive trials in the field or a critical experiment involving the inoculation of human beings with potent virus.

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## EDITORIAL

### *THE COLLEGE AND THE WAR \**

The broad educational program of the American College of Physicians was becoming firmly established as the war clouds began to gather. Rooted in the rich soil of medical science with a national faculty unsurpassed for its quality of teaching and research, the annual sessions of the College, the post-graduate courses, the regional meetings and the research fellowships were rapidly extending the influence of the College. These activities were directed to a growing body of physicians diligently bent on improving their knowledge and experience by following close on the heels of a band of brilliant teachers.

Wise leadership in the College, seeing turbulent times ahead, moved for the appointment of a Preparedness Committee before war was declared. In addition, a substantial grant was made to the Committee on Medicine of the National Research Council before funds were available from other sources for the classification and evaluation of physicians. A further grant was made to the National Research Council for the support of research and study of blood plasma at a time when funds were otherwise not forthcoming.

Medicine has a rôle of commanding importance in time of war; in fact, morale and the health of the nation are entrusted to the doctors. When the country was challenged and its security threatened, the College membership offered its services, as a body almost to the man, some to the Army, others to the Navy and still others to the Public Health Service. The latest statistics show the number on active service to be 1427 or 28.4 per cent of the entire College membership. Members of the College in a great many instances occupy responsible positions in the Medical Corps of the Services, from the Surgeons General down. Consultants in Medicine for the Pacific and European areas and the great majority of Consultants in Medicine and Allied Specialties in the eight Service Commands are Fellows of the College.

No figures suggest the large group of teachers, investigators, clinicians and others who were placed on the essential list in the country's great schools of medicine. Many of this group are now blazing new trails on assignments of far-reaching importance, serving on boards of investigation and study under the direction of the National Research Council.

Still another group from the College is contributing in a substantial manner to the war effort by serving on induction boards and in places of civilian service, many of whom were ambitious to don the uniform but, because of age limitation or some slight physical deviation, were victims of the services' rigid regulations. They also serve who stay at home!

\* The opinions and assertions contained herein are those of the author and are not to be construed as those of the Navy or of the naval service at large.

Although the annual session of the College for 1943 was cancelled, three postgraduate courses were offered, all of which were oversubscribed. The Surgeons General have encouraged available doctors to attend these courses. Civilian members have found them a beneficial respite from the wearing routine of long hours. Offering a change of atmosphere and an opportunity for an interesting review of medical advances, the postgraduate courses offered by the College may, presumably, find a higher utility in time of war, at least more so than was first thought likely.

Regional meetings in Philadelphia, Chicago, Boston, New Orleans, Washington, Great Falls, Buffalo, Kansas City, Columbus and Jacksonville, with scientific papers of the first importance, have served to stimulate interest where members of the College in the various localities mingle with members of the Services for the purpose of exchanging ideas. In considerable part the topics included in these programs have been selected because they have a distinct bearing on the war effort and present concisely the latest available knowledge on the subjects. The ANNALS OF INTERNAL MEDICINE has devoted this number exclusively to the publication of some of these papers in the belief that they will be of practical value to our younger medical officers as well as interesting to our readers generally.

Medical information created by the concentration and training of troops as well as the newer problems of medical importance arising from an accelerated industrial program is being analyzed. To these are brought the problems of civilian medicine which have gained a new importance because of the war. Preventive medicine, prophylaxis, community and individual vitality, problems of epidemiology, venereology, food supply, fatigue in industry and the services are but a few of the problems being energetically studied by members of the American College of Physicians.

The College has joined with the American Medical Association and the American College of Surgeons in the creation of a plan for mobilizing the most talented teaching personnel of the entire nation in the direction of the Army and Navy hospitals. Under the title of War-Time Graduate Medical Meetings, a committee of three doctors, one from each of the organizations sponsoring the plan, has been appointed. Funds have been appropriated to carry on the work and the program is now well under way.

A teaching faculty has been made available by the combined efforts of the three organizations whereby qualified teachers, selected by National Consultants in some 30 special fields of medicine, are now available for short intensive courses of postgraduate instruction wherever commanding officers of service hospitals desire to avail themselves of such authoritative teaching for the benefit of their respective staffs.

For the purpose of carrying on this nationwide program, the country has been divided into 24 regions and in each region a committee of three serves as a working unit for the implementation of the program. It is noteworthy that it has the authorization of the three Surgeons General.

In our nation where medical science has reached its highest pinnacle, with its great medical faculties and research institutions, leaders are being developed to carry on the work of medical reconstruction, rehabilitation and the wise distribution of medical and nutritional supplies in the war torn nations. This presupposes an international interest and point of view. Science and culture, the dual basis of medicine, know no political boundaries. Medicine needs to hold high the torch of civilization and those qualities of human existence and social welfare that make life worth living, the qualities which the world needs most at the present time. These represent the major fields of interest of the members of the American College of Physicians which explains the high percentage of the membership of the College now in positions of responsibility and importance.

Officials of the College are actively planning for the postwar period. In addition to the immediate needs of doctors for further postgraduate instruction, the encouragement of important researches and the routine life of the College must be carried on. Likewise, the College membership will be called upon to do its part in meeting the extensive needs of the devastated nations. Vision and sound planning today favor prompt action in the field of medical relief tomorrow. American Medicine is facing its greatest opportunity.

EDWARD L. BORTZ,  
Commander MC-V(S) USNR

## REVIEWS

*Synopsis of Ano-Rectal Diseases.* By LOUIS J. HIRSCHMAN. 315 pages; 13 × 20 cm. C. V. Mosby Company, St. Louis. 1942. Price, \$4.50.

This little handbook of ano-rectal diseases has been written with great care by one of wide experience in this particular field. The book is small and concise, but covers the subject thoroughly. It contains 194 fine illustrations, twelve of which are in color. In the back of the book there is a symptom index which is helpful.

The book contains a chapter on anatomy which is practical because it has been written especially for those interested in the diagnoses and treatment of ano-rectal conditions. Much space has been devoted to routine diagnostic methods used, and to routine methods of treatment. An appropriate amount of space has been devoted to methods and type of anesthesia. The chapter on focal infection of ano-rectal origin is new and enlightening.

Historical reference, bibliography, and many minute technical details have necessarily been omitted. Also the treatment of major affections of the rectum and colon, which is beyond the scope of this book, has been omitted.

It is obvious that the author has kept in mind the needs of the medical student and the general practitioner while writing this book; and because of this it is valuable, especially from a practical standpoint.

J. C. D.

*Infant Nutrition.* By WILLIAMS McKIM MARRIOTT, B.S., M.D.; Revised by P. C. JEANS, A.B. M.D. 475 pages; 15.5 × 23.5 cm. C. V. Mosby Co., St. Louis. 1941. Price, \$5.50.

The revised edition of this publication keeps it foremost among textbooks dealing with this subject.

There have been added chapters that reflect the newer pediatric thought. Growth and development have been presented in a concise manner quite suitable for the student and the practitioner. The recent advances in the various concepts of metabolic processes and vitamins have been included. The famed acid milk chapter has been improved. The various commercial preparations are nicely evaluated.

The reviewer recommends the book for the student and practitioner because of the sound information that it presents in an easily assimilable form.

J. E. B.

*Essentials of Gynecology.* By WILLARD R. COOKE, M.D., F.A.C.S. 474 pages; 16 × 23.5 cm. J. B. Lippincott Company, Philadelphia. 1943. Price, \$6.50.

This book, dealing with the essentials of gynecology, has grown out of the author's teachings and experience. The author has selected only the genuinely fundamental topics, and by that means has kept the book down to a usable size for the student and practitioner. In the chapters dealing with anatomy, embryology, abnormalities, and functional disturbances emphasis has been placed on elements of practical importance.

Throughout the book the author has included many of his own observations and his own methods of examination, and these are a valuable inclusion. Throughout the book one of the dominant considerations has been the patient as a complete personality. The important aspect of the patient's mode of life and psychology is included, and this adds something too often overlooked.

The book is 475 pages long and contains 197 illustrations, ten of which are in color. Many of the author's original line drawings are included. Most of the illustrations, particularly those of gross specimens and microphotographs, have been taken from the author's own material.

The salient features of anatomy, pathology, symptomatology, and therapy of gynecology have been well presented; and medical treatment has been stressed throughout the book. The chapter on operative gynecology is more or less an outline and is not intended for the practicing gynecologist, but is merely a guide for the student and practitioner. It includes preoperative and postoperative care and a brief outline of the more common gynecological operations.

This book is well written and is a definite expression of the author's ideas, practices, and teachings. It will serve well as a basic course for students.

J. C. D.

#### BOOKS RECEIVED

Books received during April are acknowledged in the following section. As far as practicable, those of special interest will be selected for review later, but it is not possible to discuss all of them.

*The Epidemiology of Rheumatic Fever and Some of Its Public Health Aspects.* Second Edition. By JOHN R. PAUL, M.D., and OTHER CONTRIBUTORS. 163 pages; 23.5 × 16 cm. 1943. Published by the Metropolitan Life Insurance Company for the American Heart Association.

*Mind, Medicine, and Man.* By GREGORY ZILBOORG, M.D. With a foreword by ARTHUR H. RUGGLES, M.D. 344 pages; 22 × 15 cm. 1943. Harcourt, Brace and Company, New York, N. Y. Price, \$3.50.

*A Text-Book of Pathology.* Fourth Edition. Thoroughly Revised. By WILLIAM BOYD (M.D., LL.D., M.R.C.P., Ed., F.R.C.P., Lond., Dipl. Psych., F.R.S.C.). 1008 pages; 24 × 15.5 cm. 1943. Lea and Febiger, Philadelphia. Price, \$10.00.

*Methods for Diagnostic Bacteriology.* Second Edition. By ISABELLE G. SCHAUB, A.B., and M. KATHLEEN FOLEY, A.B. 430 pages; 22 × 14.5 cm. 1943. C. V. Mosby Company, St. Louis, Missouri. Price, \$3.50.

*Neurology.* Third Edition. By ROY R. GRINKER, M.D. 1136 pages; 25.5 × 17 cm. 1943. Charles C. Thomas, Springfield, Illinois. Price, \$6.50.

*La Urobilina en el Estado Normal y Patologico.* Segunda Edicion. By MARCELO ROYER. 265 pages; 23 × 16 cm. 1943. El Ateneo, Buenos Aires, Argentina.

*Primer of Allergy.* Second Edition. By WARREN T. VAUGHAN, M.D. 176 pages; 20 × 13 cm. 1943. C. V. Mosby, St. Louis, Missouri. Price, \$1.75.

*A Manual of Otology, Rhinology and Laryngology.* Second Edition. By HOWARD CHARLES BALLENGER, M.D., F.A.C.S. 334 pages; 24 × 15 cm. 1943. Lea and Febiger, Philadelphia. Price, \$4.00.

*Clinical Significance of the Blood in Tuberculosis.* By GULLI LINDH MULLER, M.D. 516 pages; 24 × 16 cm. 1943. The Commonwealth Fund, New York, N. Y. Price, \$3.50.

*Hope Deferred.* By JEANETTE SELETZ. 536 pages; 22 × 15 cm. 1943. The Macmillan Co., New York, N. Y. Price, \$2.75.

*Victories of Army Medicine.* By EDGAR ERSKINE HUME, Colonel, Medical Corps, U. S. Army. 250 pages; 24 × 15.5 cm. 1943. J. B. Lippincott Company, Philadelphia. Price, \$3.00.



## COLLEGE NEWS NOTES

### ADDITIONAL A. C. P. MEMBERS IN THE ARMED FORCES

Already published in preceding issues of this journal were the names of 1,411 Fellows and Associates of the College on active military duty. Herewith are reported the names of 19 additional members, bringing the grand total to 1,430.

George O. Bell  
Philip G. C. Bishop  
Franklin G. Ebaugh  
Eugene Eisner  
George N. Furbeck  
Lewis P. Gundry  
Adolph M. Hutter  
John S. Kapernick  
Richard J. Killhullen  
Robert C. Levy

Frank X. Marino  
Currier McEwen  
Joseph Mignone  
Frank T. Moore  
Benjamin H. Neiman  
Samuel Nesbitt  
H. Milton Rogers  
James M. Strang  
Donald M. Willson

Dr. George A. Cann, F.A.C.P., has been retired from active duty in the Medical Corps of the U. S. Naval Reserve because of physical disability and has returned to private practice in Reno, Nev.

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### NEW LIFE MEMBERS OF THE COLLEGE

The following Fellows of the American College of Physicians have subscribed to Life Membership, and their initiation fees and Life Membership subscriptions have been added to the permanent Endowment Fund of the College:

Dr. Archibald Lawrence Hoyne, Chicago, Ill.  
Dr. Edgar Paul McNamee, Cleveland, Ohio

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### GIFTS TO THE COLLEGE LIBRARY

We gratefully acknowledge receipt of the following gifts to the College Library of Publications by Members:

#### *Books*

- Franklin G. Ebaugh, F.A.C.P., Colonel, (MC), U. S. Army—"Psychiatry in Medical Education";  
Dr. Oswald F. Hedley, F.A.C.P., U. S. Public Health Service, Bethesda, Md.—"Manual of Industrial Hygiene";  
Dr. David O. N. Lindberg, F.A.C.P., Oakdale, Iowa—"A Manual of Pulmonary Tuberculosis and an Atlas of Thoracic Roentgenology";  
Dr. Francis P. McNamara, F.A.C.P., Dubuque, Iowa—"Collected Reprints of the Medical Staff of Finley Hospital";  
Dr. LeRoy Sante, F.A.C.P., St. Louis, Mo.—"Manual of Roentgenological Technique, 1943" and "Principles of Roentgenological Interpretation, 1942";  
Dr. Alexander S. Wiener (Associate), Brooklyn, N. Y.—"Blood Groups and Transfusion."

*Reprints*

Dr. Leon L. Blum (Associate), Terre Haute, Ind.—1 reprint;  
Joseph G. Bohorfoush, F.A.C.P., Major, (MRC), U. S. Army—1 reprint;  
Dr. Verne S. Caviness, F.A.C.P., Raleigh, N. C.—4 reprints;  
Dr. Donald R. Chisholm (Associate), Kealia, Kauai, T. H.—4 reprints;  
Irving Ershler (Associate), Captain, (MRC), U. S. Army—3 reprints;  
Dr. O. P. J. Falk, F.A.C.P., St. Louis, Mo.—1 reprint;  
Dr. Robert H. Flinn (Associate), U. S. Public Health Service, Chicago, Ill.—2 reprints;  
John Langdon Gompertz (Associate), Captain, (MRC), U. S. Army—1 reprint;  
Dr. William E. Jahsman, F.A.C.P., Ferndale, Mich.—2 reprints;  
Dr. Abraham M. Litvak, F.A.C.P., Brooklyn, N. Y.—2 reprints;  
Samuel Millman, F.A.C.P., Major, (MRC), U. S. Army—2 reprints;  
Dr. William H. Ordway, F.A.C.P., Mount McGregor, N. Y.—1 reprint;  
Dr. Hyman I. Spector, F.A.C.P., St. Louis, Mo.—7 reprints;  
Dr. Alexander S. Wiener (Associate), Brooklyn, N. Y.—7 reprints.

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Dr. Edward A. Strecker, F.A.C.P., Philadelphia, Pa., has been named a Consultant in Psychiatry to the Bureau of Medicine and Surgery of the U. S. Navy.

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Dr. Henry A. Luce, F.A.C.P., Detroit, Mich., was recently installed as President of the Michigan Society of Neurology and Psychiatry.

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Dr. Carl J. Wiggers, F.A.C.P., Cleveland, Ohio, spoke on "Recent Studies of the Irreversibility Characteristic of Shock" at a meeting of the Detroit Physiological Society, March 18. On March 26 Dr. Wiggers addressed a meeting of the Michigan Academy of Science, Ann Arbor, Mich., on "Recent Observations on the Value of Adrenal Cortex Preparations in Hemorrhagic Shock" and on April 13 presented the Adam Miller Lecture at the Long Island College of Medicine, Brooklyn, N. Y., on "Recent Experimental Approaches to the Shock Problem."

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The 3rd Annual Meeting of the American Diabetes Association, 1943, has been cancelled.

Dr. Joseph T. Beardwood, Jr., F.A.C.P., Philadelphia, Pa., is the President; Dr. Joseph H. Barach, F.A.C.P., Pittsburgh, Pa., is 1st Vice President; Dr. Russell M. Wilder, F.A.C.P., Rochester, Minn., 2nd Vice President; and Dr. Cecil Striker, F.A.C.P., Cincinnati, Ohio, Secretary. Dr. Elliott P. Joslin, F.A.C.P., of Boston, Mass., is the Honorary President.

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John Dibble, F.A.C.P., Colonel, (MC), U. S. Army, has been reported missing in an airplane accident in the southern Pacific area, according to an announcement made in April of this year.

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Dr. Walter E. Vest, F.A.C.P., Huntington, W. Va., has been appointed Acting Governor for West Virginia to succeed Dr. Albert H. Hoge, F.A.C.P., Bluefield, who died on April 9, 1943.

Among the speakers at a Clinical Research Meeting arranged by the Committee on Medical Education of the New York Academy of Medicine were the following members of the College:

- Dr. Arthur W. Grace, F.A.C.P., New York, N. Y., "The Complement-Fixation Test for Lymphogranuloma Venereum; Results Obtained with Its Use";
  - Dr. Thomas H. McGavack, F.A.C.P., New York, N. Y., "Neurohormonal Regulation of Water Balance: Studies in Patients with Diabetes Insipidus";
  - Dr. Randolph West, F.A.C.P., New York, N. Y., "Nitrogen Retention, Creatinuria, and Other Effects of the Treatment of Simmonds' Disease with Methyl Testosterone";
  - Dr. Linn J. Boyd, F.A.C.P., New York, N. Y., "The Effect of Sodium Thiosulphate on the Blood";
  - Dr. Leo Loewe (Associate), Brooklyn, N. Y., "A New Practical Method for the Subcutaneous Administration of Heparin."
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James S. Simmons, F.A.C.P., Brigadier General, (MC), U. S. Army, Director of the Preventive Medicine Division, Office of the Surgeon General, delivered the John Wyckoff Lectures at New York University on April 15 and 16, 1943. General Simmons spoke on "The Preventive Medicine Program of the United States Army"; "The Present State of the Army's Health."

General Simmons was recently appointed Lecturer in Public Health at Yale University School of Medicine.

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Among the speakers at the 52nd Annual Meeting of the Arizona State Medical Association held in Tucson, April 30-May 1, were Dr. Charles S. Kibler, F.A.C.P., Tucson, who spoke on "Demonstration of Heart Disease" and Dr. Earle W. Phillips, F.A.C.P., Phoenix, "Relief of Allergic Premenstrual Headache."

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Dr. George Blumer, F.A.C.P., New Haven, Conn., presented the annual George Dock Lecture of the Barlow Society for the History of Medicine at a meeting of the Los Angeles County Medical Association in Los Angeles, Calif., April 2. Dr. Blumer spoke on "Remarks on the Life and Accomplishments of William Heberden the Younger."

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The California Medical Society held its 72nd Annual Session in Los Angeles, May 2-3. Among the speakers were:

- Dr. John H. Fitzgibbon, F.A.C.P., Portland, Ore., "Wartime Community Health Problems in Oregon";
  - Dr. Tom D. Spies, F.A.C.P., Birmingham, Ala., "Detailed Methods of Diagnosis and Therapy in Acute Nutritive Failure."
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Dr. Edward A. Strecker, F.A.C.P., Philadelphia, Pa., spoke on "Something on Therapy in Alcoholic Conditions" and Dr. Harold G. Wolff, F.A.C.P., New York, N. Y., spoke on "Emotions and Disease" at a recent series of lectures sponsored by the Graduate Club of the Neuro-Psychiatric Institute of the Hartford Retreat, Hartford, Conn.

The Graduate School of the University of Florida has established a new Department of Medicine, which will be located in Jacksonville and maintained in coöperation with the Medical Society of the State of Florida and the State Board of Health. Dr. Turner Z. Cason, F.A.C.P., College Governor for Florida, Jacksonville, has been named Director of the Department. The new unit will conduct graduate courses and promote research in medicine and surgery. Continuation courses with facilities for clinical instruction for practicing physicians will also be given periodically.

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The California Heart Association held its annual meeting in Los Angeles, May 1. Among the speakers were:

Dr. Samuel J. McClendon, F.A.C.P., San Diego, "The Incidence of Acute Rheumatic Fever in Southwestern United States";

Richard F. McLaughlin, F.A.C.P., Lieutenant Commander, (MC), U. S. Naval Reserve, "Rheumatic Infection in a Plateau Area."

Guest speakers at this meeting of the Association were Dr. George Blumer, F.A.C.P., New Haven, Conn., and Dr. Alvin G. Foord, F.A.C.P., Pasadena.

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The 151st Annual Meeting of the Connecticut State Medical Society was held in New Haven under the Presidency of Dr. Roy L. Leak, F.A.C.P., Middletown. Among the Fellows of the College who participated were:

Dr. George H. Gehrmann, F.A.C.P., Wilmington, Del., "Medicine in Wartime Industry";

Dr. James E. Paullin, F.A.C.P., Atlanta, Ga., President of the College, "The Contribution of the Medical Profession in the Present War Effort";

Dr. John D. Currence, F.A.C.P., New York, N. Y., "Arthritic and Rheumatic Conditions Amenable to Physical Therapy";

Dr. Willard C. Rappleye, F.A.C.P., New York, N. Y., "Medical Education in Wartime";

Bartholomew W. Hogan, F.A.C.P., Commander, (MC), U. S. Navy, "Navy Medical Corps in Wartime."

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Among the guest speakers at the annual meeting of the Medical Society of the State of New York held in Buffalo, May 3-6, were:

Dr. George Baehr, F.A.C.P., Chief Medical Officer, Office of Civilian Defense, Washington, D. C., "British and American Experiences in Civil Defense";

Thomas T. Mackie, F.A.C.P., Lieutenant Colonel, (MRC), U. S. Army, "Tropical Diseases—A Postwar Health Problem."

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The New York Heart Association recently formed a Committee on Cardiovascular Diseases in Industry, to aid industry in determining employability of persons with cardiovascular diseases. Dr. Clarence E. de la Chapelle, F.A.C.P., is Chairman of this Committee and Dr. Oswald F. Hedley, F.A.C.P., U. S. Public Health Service, Bethesda, Md., is one of its members.

Dr. Albert E. Russell, F.A.C.P., U. S. Public Health Service, Governors Island, N. Y., spoke on "Silicosis" at the 90th Annual Session of the Minnesota State Medical Association held in Minneapolis May 17-19.

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Dr. Charles C. Bass, F.A.C.P., New Orleans, La., delivered the Ewing Fox Howard Oration at a public session conducted by the Mississippi State Medical Association during their 76th Annual Session in Jackson, May 12-13. Dr. Bass spoke on "Prevention of the Loss of Teeth."

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Dr. Roger I. Lee, F.A.C.P., Boston, Mass., spoke on "Geriatrics: The Medical Care of the Elderly" at the 152nd Annual Meeting of the New Hampshire Medical Society in Manchester, May 11.

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The New York Academy of Medicine has organized a Committee to Study Medicine and the Changing Order. The objectives of this Committee are "to be informed on the nature, quality and direction of the economic and social changes that are taking place now and that are clearly forecast for the immediate future; to define in particular how these changes are likely to affect medicine in its various aspects; to determine how the best elements in the science of medicine and its services to the public may be preserved and embodied in whatever changed social order may ultimately develop." Dr. James Alexander Miller, M.A.C.P., Dr. Arthur F. Chace, F.A.C.P., Dr. I. Ogden Woodruff, F.A.C.P., all of New York, N. Y., Dr. Jean A. Curran, F.A.C.P., Brooklyn, and Dr. George Baehr, F.A.C.P., Washington, D.C., have been named members of this Committee.

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Philip W. Brown, F.A.C.P., Major, (MRC), U. S. Army, spoke on "Amebiasis" and Dr. W. Reece Berryhill, F.A.C.P., Chapel Hill, N. C., spoke on "Atypical Pneumonia of Unknown Etiology" at the 90th Annual Session of the Medical Society of the State of North Carolina held in Raleigh, May 10-12.

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Dr. Harold M. Coon, F.A.C.P., Madison, Wis., was recently elected President of the Wisconsin Hospital Association.

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Dr. Samuel B. Hadden, F.A.C.P., Philadelphia, Pa., spoke on "Group Psychotherapy" at the annual meeting of the American Neurological Association in New York, N. Y., May 6-7.

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The Illinois State Medical Society held its 103rd Annual Meeting in Chicago, May 18-20. Among the guest speakers were Dr. Paul A. O'Leary, F.A.C.P., Rochester, Minn., who spoke on "Wartime Considerations of Syphilis" and Dr. James E. Paullin, F.A.C.P., President of the College, Atlanta, Ga., who delivered the annual Oration in Medicine.

Dr. John R. Vonachen, F.A.C.P., Peoria, Ill., participated in a symposium on "Nutrition" and Dr. Francis D. Murphy, F.A.C.P., Milwaukee, Wis., and Dr. Edgar



M. Stevenson, F.A.C.P., Bloomington, Ill., conducted a round table discussion on "Cardiovascular Diseases."

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The Massachusetts Medical Society held its 162nd Annual Meeting in Boston, May 24-26. Among the guest speakers were:

Dr. Thomas Parran, F.A.C.P., The Surgeon General, U. S. Public Health Service, "Wartime Responsibilities of the Public Health Service";

James S. Simmons, F.A.C.P., Brigadier General, (MC), U. S. Army, "Global Malaria";

Dr. Russell M. Wilder, F.A.C.P., Washington, D. C., "Medical Nutritional Requirements in the Time of War";

Dr. Alvan L. Barach, F.A.C.P., New York, N. Y., "Oxygen Therapy, as Related to Gas Poisoning in War and in Civilian Disasters."

Dr. George W. Thorn, F.A.C.P., Boston, delivered the Shattuck Lecture on "Physiological Considerations in the Treatment of Nephritis," May 25.

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The Merck Institute for Therapeutic Research, Rahway, N. J., a nonprofit corporation founded in 1933 to conduct investigations into the causes, nature and mode of prevention and cure of diseases in men and animals, recently commemorated its tenth anniversary. Among the speakers at the anniversary ceremonies were Dr. William H. Sebrell, Jr., F.A.C.P., U. S. Public Health Service, Bethesda, Md., Dr. Francis G. Blake, F.A.C.P., New Haven, Conn., and Dr. Russell M. Wilder, F.A.C.P., Washington, D. C.

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The Journal of the Bowman Gray School of Medicine of Wake Forest College, Winston-Salem, N. C., will be published bimonthly by the students of the medical school. The first issue of this new journal was dedicated to Dr. Coy C. Carpenter, F.A.C.P., Dean of the medical school for his assistance in making this journal possible.

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Dr. Waller S. Leathers, F.A.C.P., Nashville, Tenn., was recently elected President of the Basic Science Board of Tennessee, and Dr. Edward L. Turner, F.A.C.P., Nashville, Vice President.

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Among the speakers at the 76th Annual Meeting of the West Virginia State Medical Association in Charleston, May 16-18, were:

Dr. William H. Sebrell, Jr., F.A.C.P., U. S. Public Health Service, Bethesda, Md., "Maintaining Adequate Nutrition in Wartime";

Dr. A. Wilbur Duryee, F.A.C.P., New York, N. Y., "Peripheral Vascular Disease and Industry."

Dr. Edward J. Van Liere, F.A.C.P., Dean of the West Virginia University School of Medicine, Morgantown, delivered the Oration on Medicine. Dr. Van Liere spoke on "The Effect of Anoxia on the Body."

Hugh R. Butt, F.A.C.P., Lieutenant, (MC), U. S. Naval Reserve, spoke on "Gastric and Duodenal Ulcers in the Naval Personnel" and Dr. Lewis M. Hurxthal, F.A.C.P., Boston, Mass., on "The Thyrocardiac—A Review of Six Hundred Cases" at the annual meeting of the American Surgical Association in Cincinnati, Ohio, May 13-14.

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The 8th Annual Postgraduate Institute of the Philadelphia County Medical Society on the "Management of Emergencies" was held in Philadelphia, Pa., May 11-14, 1943. Among the Philadelphia members of the College who participated in the program were:

- Dr. William P. Belk, F.A.C.P., "The Wassermann Test, Blood Sedimentation Test, Plasma Balance in Emergencies";
- Dr. John Eiman, F.A.C.P., "Coma from the Urologist's Point of View";
- Dr. George Morris Piersol, F.A.C.P., "Coma from the Internist's Point of View";
- Dr. Charles L. Brown, F.A.C.P., "Diagnosis and Treatment of Acute Cerebral Vascular Accidents";
- Dr. Harold W. Jones, F.A.C.P., "Agranulocytosis and Hemorrhagic Diseases";
- Dr. Harrison F. Flippin, F.A.C.P., "Treatment of Septicemia";
- Dr. George E. Pfahler, F.A.C.P., "Roentgen Ray Treatment of Acute Inflammatory Conditions";
- Dr. Stanley P. Reimann, F.A.C.P., "Blood Counts, Urinalysis Examination, Blood Typing and Pneumococcus Typing in Emergencies";
- Dr. John A. Kolmer, F.A.C.P., "Treatment of Acute Bacterial Meningitis";
- Dr. Henry L. Bockus, F.A.C.P., "Acute Diarrheas";
- Dr. William D. Stroud, F.A.C.P., "Diagnosis and Treatment of Acute Coronary Occlusion";
- Dr. Charles C. Wolferth, F.A.C.P., "Diagnosis and Treatment of Angina Pectoris";
- Dr. Russell S. Boles, F.A.C.P., "Prevention and Medical Management of Acute Complications of Ulcer";
- Dr. W. Edward Chamberlain, F.A.C.P., "The Roentgen Analysis of Fractures";
- Dr. Thomas M. McMillan, F.A.C.P., "Diagnosis and Treatment of Acute Pulmonary Edema";
- Dr. William G. Leaman, Jr., F.A.C.P., "Diagnosis and Treatment of Acute Congestive Heart Failure";
- Dr. Louis H. Clerf, F.A.C.P., "Foreign Bodies in the Bronchial Air Passages."

Dr. A. Hamilton Stewart, F.A.C.P., Secretary of Health of the Commonwealth of Pennsylvania, Harrisburg, and Dr. Augustus S. Kech, F.A.C.P., President-Elect of the Medical Society of the State of Pennsylvania, Altoona, were among the guest speakers at the opening day luncheon of the Society.

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The 51st Annual Session of the Oklahoma State Medical Association was held in Oklahoma City, May 11-12, 1943. Among the speakers were:

- Udo J. Wile, F.A.C.P., Colonel, U. S. Public Health Service, Ann Arbor, Mich., "The Rapid Treatment Method for Syphilis";
- Dr. Coyne H. Campbell, F.A.C.P., Oklahoma City, "Demonstration of Minimum Neuropsychiatric Examination for Inductees";
- Dr. Charles E. Leonard (Associate), Oklahoma City, "Demonstration of Minimum Neuropsychiatric Examination for Inductees";

- Dr. C. W. Arrendell, F.A.C.P., Ponca City, "The Child in the Local Health Program";  
 William H. Gordon, F.A.C.P., Colonel, (MRC), U. S. Army, "Neutropenias";  
 Dr. Homer A. Ruprecht, F.A.C.P., Tulsa, "Unusual Findings in Coronary Disease";  
 Dr. J. William Finch, F.A.C.P., Hobart, "Androgenic Therapy in the Female";  
 Leslie B. Marshall (Associate), Captain, (MC), U. S. Navy, "Naval Medicine";  
 Dr. Wann Langston, F.A.C.P., Oklahoma City, "Some Observations on Coronary Disease";  
 W. Lee Hart, F.A.C.P., Colonel, (MC), U. S. Army, "Activities of the Medical Department in the Eighth Service Command."

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The Medical Association of Georgia held its 94th Annual Session in Atlanta, May 11-14, 1943. Guest speakers on the scientific program included:

- Dr. Chauncey C. Maher, F.A.C.P., Chicago, Ill., "Complications of Acute Coronary Thrombosis";  
 Dr. James H. Means, F.A.C.P., Boston, Mass., "Practical Points in the Diagnosis and Treatment of Graves' Disease" and "Some Features of Peptic Ulcer."

The Abner Wellborn Calhoun Lecture of the Association was delivered by Ross T. McIntire, F.A.C.P., Rear Admiral, (MC), U. S. Navy, The Surgeon General. Admiral McIntire spoke on "Medical Achievements in This Present War."

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Dr. Salvador Zubiran, F.A.C.P., Mexico City, D. F., is the President of the First National Congress of Public Welfare, called by the President of Mexico, to be held in the City of Mexico, August 15-22, 1943. It is the desire of the officers planning this Congress that leaders in the fields of medicine and public welfare throughout the continent shall attend and thus strengthen the ties of friendship and mutual understanding.

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#### REGIONAL MEETING ATTENDANCE

The attendance at three recent Regional Meetings of the American College of Physicians is revealed in the statistics that follow. Each meeting presented an excellent program, yet varying in content and in the speakers presenting papers. It is felt that no single war-time activity of the College has been of such widespread value as these Meetings. Ordinarily, at Annual Sessions, there is a participation by approximately 20 to 23 per cent of the College membership. The average participation by members at these Regional Meetings has been about 40 to 42 per cent.

The attendance record for three recent Meetings follows (Washington, D. C., April 24, 1943—Delaware, Maryland, District of Columbia, Virginia, North Carolina and West Virginia; Kansas City, May 8, 1943—Missouri, Kansas, Oklahoma and Nebraska; Columbus, May 14, 1943—Ohio, Kentucky, West Virginia and Western Pennsylvania):

	Members	% of Membership	Guests	TOTAL	Civilian Doctors	Army	Navy	U.S.P.H.S.
Washington....	263	45.5	200	463	200	177	75	11
Kansas City....	109	42.4	164	273	172	89	7	5
Columbus.....	113	27.0	107	220	166	48	4	2

The State of Kansas at the Kansas City Meeting led all other States with a member attendance of 68.6 per cent. At the Washington Meeting, Maryland led with a member attendance of 52.5 per cent. At the Columbus Meeting, Kentucky led with a member attendance of 34.8 per cent.

#### WAR-TIME GRADUATE MEDICAL MEETINGS

A "Statement of Organization" of the War-Time Graduate Medical Meetings appeared in these columns in the May, 1943, issue. That announcement not only outlined the objectives and purposes of the Central Committee, consisting of Comdr. Edward L. Bortz, Chairman, Philadelphia, Pa., Dr. William B. Breed, Secretary-Treasurer, Boston, Mass., and Dr. Alfred Blalock, Baltimore, Md., but explained the method of operation and delineated the duties of the Section Committees and the Board of Consultants. The program is authorized by the Surgeons General of the U. S. Army, the U. S. Navy and the U. S. Public Health Service, and is a joint project of the American Medical Association, the American College of Physicians and the American College of Surgeons. The organization is national in scope and proposes to organize and conduct graduate instruction in the form of ward walks, clinics, demonstrations, lectures, round tables and conferences to large medical installations in the Armed Forces throughout the nation. The Central Committee has already initiated some of the programs and is now prepared to organize programs at any Service Hospital in which there is a reasonably large number of medical officers and from the commanding officer of which a request is filed for such programs.

Herewith published is the personnel of the Board of National Consultants and the personnel of the Regional Committees.

#### *Board of National Consultants*

1. ALLERGY ..... Robert A. Cooke, F.A.C.P.  
New York, N. Y.
2. ANESTHESIA ..... John S. Lundy  
Rochester, Minn.
3. AVIATION MEDICINE ..... W. Paul Holbrook, F.A.C.P.  
Lt. Col., (MC), U.S.A.  
Washington, D. C.
4. CARDIOVASCULAR PROBLEMS ..... William D. Stroud, F.A.C.P.  
Philadelphia, Pa.
5. CHEMOTHERAPY ..... Chester S. Keefer, F.A.C.P.  
Boston, Mass.
6. DERMATOLOGY ..... Chester N. Frazier, F.A.C.P.  
Baltimore, Md.
7. DYSENTERIES ..... Thomas T. Mackie, F.A.C.P.  
Lt. Col., (MC), U.S.A.  
Washington, D. C.
8. EPIDEMIOLOGY AND LABORATORY MEDICINE.. Roy R. Kracke  
Decatur, Ga.
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## OBITUARIES

## DR. F. B. WATKINS

In the recent death of Dr. F. B. Watkins the American College of Physicians has suffered the loss of a distinguished member. A native of Rutherford County, North Carolina, Fonso Butler Watkins was born April 12, 1878, son of Galeb Whicker and Quintina Wallace Watkins. He was graduated from the University of North Carolina in 1900, and was a member of Phi Beta Kappa. After teaching school for a time in the State of Georgia, he entered the Jefferson Medical College, where he graduated in 1907. He then served an internship in Philadelphia, after which he entered practice in Concord, North Carolina. He remained in private practice only six months, when he joined the staff of the State Hospital in Morganton, where he served continuously for thirty-three years. During his stay at the Morganton institution, he served as assistant superintendent until 1938 when he became superintendent of the institution.

Dr. Watkins was prominent in professional circles and reflected credit upon all organizations to which he belonged. At the time of his death he was President of the North Carolina Neuro-Psychiatric Society. Being of a retiring nature, Dr. Watkins was not intimately known by a large number of people. Those who did know him, however, were rewarded by a worthy, a sincere, and a loyal friendship. He was genuinely respected by his colleagues and his friends throughout the State in which he lived and labored. By his sterling worth he has left a rich heritage to his wife, Mrs. Helen Watrous Watkins and his son, William Downing Watkins, who like his father, is preparing himself for a medical career at the University of North Carolina.

In declining health for some time, he bore bravely and with fortitude an investigation of the institution which he headed, an investigation which was brought about through no fault of his own, and which left his sterling character unblemished. Although his sensitive nature must have suffered, like the good soldier that he was, he suffered in silence.

A fitting tribute to Dr. Watkins is the following editorial from the Winston-Salem Journal and Sentinel, entitled "Able State Servant."

"The death of Dr. F. B. Watkins, superintendent of the Western Hospital for the Insane, at a Rutherfordton hospital, removes from the service of the State one of its ablest servants.

"It is significant that while the State Hospital at Morganton has been subjected to much publicity of an adverse nature during the past two years, no breath of scandal or charges of incompetence or negligence involved Dr. Watkins. His difficulties at Morganton were apparent to all who knew anything about the mental institution which he headed. Like the Israelites who were enslaved by the Pharaohs in Egypt, he was forced to 'make brick without straw.' And in the face of tremendous odds and severe handicaps he did accomplish remarkable results.

"Dr. Watkins was genial, humane, sympathetic of manner, a keen student of psychiatry. He knew human nature, normal and abnormal. He resisted the lure of private practice to devote his life to the cause of the most helpless and in many cases the most hopeless wards of the commonwealth, and for many years as assistant to the superintendent, and as superintendent, endeavored to do the work of two or three psychiatrists and physicians, at the same time doing a prodigious amount of executive work.

"No doubt this over-exertion is one reason why Dr. Watkins is dead at the age of 64. The State of North Carolina owes much to this selfless minister to minds diseased, and there are many beneficiaries of his ministrations who will today rise up in many sections of the State to call him blessed."

The American College of Physicians was honored to count Dr. Watkins among its Fellows, and with his family and friends feels a genuine loss in his passing.

PAUL F. WHITAKER, M.D., F.A.C.P.,  
Governor for North Carolina

#### DR. JOHN WILLIAM STOFER

Dr. John William Stofer, F.A.C.P., a long honored physician of Gallup, New Mexico, died January 16, 1943, at the age of sixty-four of cerebral hemorrhage. Dr. Stofer received his M.D. degree at the University Medical College of Kansas City in 1908 and a year later came to Gallup. He lived and practiced there continuously, with the exception of one year, 1916-17, until about a year before his death when ill health forced his retirement.

Dr. Stofer was for many years on the Staff of St. Mary's Hospital. He had served as President of the McKinley County Medical Society and of the New Mexico Medical Society and had been a Fellow of the American College of Physicians since 1931. He was interested in Masonic affairs and, while taking part in many of the social activities of his professional associations, was more interested in his professional work. His loss is felt as a friend, and as a highly esteemed and faithful physician.

ROBERT O. BROWN, M.D., F.A.C.P.,  
Governor for New Mexico

#### DR. ARCHIBALD S. DENNISON

Dr. Archibald S. Dennison, F.A.C.P., died suddenly January 22, 1943, at his home in Lynn, Massachusetts. Although his health had been failing for months, he kept up his active practice until the day before his death. Born in Bridgetown, Nova Scotia, in 1869 Dr. Dennison went to Lynn in his early youth and spent his entire professional life in that city where he practiced as a well-loved family physician up to the time of his death. His professional standing locally, as well as with the medical fraternity of Greater Boston, was high.

Dr. Dennison's professional education was acquired in the Bellevue Hospital Medical College where he received an M.D. degree in 1896. For many years he was an active and honorary member of the medical staff of the Lynn Hospital. Dr. Dennison was elected to Fellowship in the American College of Physicians in 1921 and was also a member of the New England Pediatric Society, the Massachusetts Medical Society, and a Fellow of the American Medical Association.

Dr. Dennison is survived by a daughter, Barbara, and a son, Frederick C. Dennison, M.D., of Thomaston, Maine, who is now serving in Alabama as Lieutenant in the Army Air Force.

WILLIAM B. BREED, M.D., F.A.C.P.,  
Governor for Massachusetts

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*Erratum.* In the article by Dr. David I. Macht on "Experimental Studies on Heparin and Its Influence on Toxicity of Digitaloids, Congo Red, Cobra Venom and Other Drugs" in the ANNALS OF INTERNAL MEDICINE, May 1943, page 782, an error was made in the illustration. In preparing the plate, the upper portion of the original photograph was cut away, and with this the tracing of the respirations during the experiment. The figure will be published in correct form in the author's reprints. We regret the error.





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